VOLUME 14 NUMBER 3

ENDOCRINOLOGY

THE BULLETIN OF THE ASSOCIATION
FOR THE STUDY OF

INTERNAL SECRETIONS

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MAY-JUNE

1930

PUBLISHED BI-MONTHLY BY THE ASSOCIATION FOR THE STUDY OF INTERNAL SECRETIONS, SUITE 1214 WILSHIRE MEDICAL BLDG., LOS ANGELES, CALIFORNIA
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ENDOCRINOLOGY

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INTERNAL SECRETIONS

Volume 14, Number 3 MAY-JUNE, 1930 Serial No. 71

ENDOCRINOLOGY AND NEUROLOGY*

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Fellow members and guests of the Association for the Study of Internal Secretions: Our fourteenth annual meeting opens under auspicious circumstances. We are assembled in a city in the center of the continent, an important center for research in the field of endocrinology and for the manufacture and distribution of endocrine products. Here in Detroit we can not only listen to accounts of work done, ask questions and utter criticisms, but we may visit able investigators in their laboratories and witness precise manufacturing technique based upon the investigations of these scientists. This location is ideal also for the exchange of ideas between the two largest nations on this continent. We of the United States owe an expression of homage, admiration and gratitude to our neighbors on the north, who within a period of a few years have given insulin and parathyroid hormone to the world. However, we may permit ourselves to point with some pride to recent achievements in connection with the hypophysis, thyroid, adrenals and gonads. That our Association, its annual meetings and its journal are growing in importance and commanding increasing serious attention and confidence is apparent. As a sign of growth I call your attention to the size and scope of the program of this meeting, and I am confident that its high quality will speak for itself. This is the first time that your officers have ventured to invite you to spend two days at our meeting, and they have done so with the conviction that it is justified by the quantity and quality of new research to be presented.

The one ironical and malapropos feature of this meeting is the fact that its presiding officer is the only participant in the program who is devoid of distinction as an investigator in the field which this Association represents. At previous meetings he has never been more than an humble but interested listener, who always has felt amply rewarded by information acquired which has helped him in his daily work as a practitioner and teacher of neurology. The close interrelationship between endocrinology and neurology has been personified in three of his predecessors, Barker, Cushing and Timme, all of whom, unlike the present incumbent, have made important contributions in both fields.

*President's Address at the Fourteenth Annual Meeting of the Association for the Study of Internal Secretions, Detroit, Mich., June 23, 1930.

Neurologists are often, and sometimes justly, accused of being speculative, verbose, and afflicted with a cumbersome nomenclature, but they must be given credit for having early understood the importance of the part played by the organs of internal secretion. Long ago the neurologist, Wagner-Jauregg of Vienna, said that organotherapy is not only a field for research but should itself be a means of research. An example is the amazing production of many nervous and mental syndromes by insulin reactions. Many a neurologist unfamiliar with these reactions has seen his reputation suffer on account of his failure to keep abreast of the progress of endocrine therapy. Psychiatrists are grateful to the discoverers of insulin because they find it a useful drug for undernourished, depressed patients. The permanent benefit from insulin in such cases makes up many fold for the occasional production of transient nervous and mental symptoms in diabetics. Without knowledge of the action of insulin we should not have learnt to understand the pathogenesis of convulsions and coma in cases of adenoma of the islands of Langerhans. Thus, we here have seen Wagner-Jauregg's prophecy come true. A few years ago it began to look as if it were going to be admitted that the endocrines regulated everything from menses and hibernation to personality, poetry and politics. However, a reaction has come, and now two or three new regulating centers in the hypothalamic region are being discovered (or imagined), for every new hormone. Mauthner's old idea of a sleep center has been revived. Thirst, diuresis, adiposity and emaciation are made and unmade by manipulating the hypothalamus regardless of the hypophysis, both in its absence and in its presence. Centers controllnig not only water, sugar and fat metabolism but protein metabolism and basal metabolism are now described by physiologists. I shall confine myself to pointing out briefly some of the contributions of neuropathology and clinical neurology to these problems. Observations on epidemic encephalitis, particularly its chronic forms, have taught us that lesions of the brain may cause many symptoms and syndromes formerly considered due only to lesions of the hypophysis, notably diabetes insipidus and adiposis with genital atrophy. However, detailed anatomic investigations are still few. Felix Stern (1) observed adiposis in 39 of 500 cases and attributes it to lesions of the tuber cinereum. It is noteworthy that he occasionally observed regression of both the adiposis and genital atrophy. Pubertas praecox, preceded by salivation and parkinsonism, has been described by Stern (2), John (3) and Wimmer (4). The frequency of hyperidrosis and increased sebaceous secretion (''greasy face,'' ''Salbengesicht'') in encephalitis is of interest in connection with Lotmar's idea of a sweat center in the posterior medial portion of the thalamus and L. R. Müller and Greving's center for sebaceous secretion in the tuber cinereum. Riese (5) observed a young woman with encephalitic rigidity, obesity, considerable sexual excitement and colostrum-like secretion from the breasts which had been present over five years. He ascribes this to disorder of vegetative brain centers. Increased basal metabolic rate is fairly common both in chronic parkinsonian encephalitis and in true paralysis

agitans. One of the largest groups of patients tested is that reported by Naccarati (6). Of 47 chronic encephalitic patients 28 showed altered rate, 25 increased, 3 decreased. There was no relationship between the degree and extent of tremor and the basal rate, which is an argument against the theory that increased muscular activity is the cause of increase in basal rate. Extensive animal experiments over a period of years by Steinhaus (7) also failed to support the muscular theory. Other explanations offered are that actual activation of the thyroid occurs or that a certain center in the interbrain is affected by the pathologic process. Gräfe and Grünthal (8) have performed experiments on dogs which led them to believe that basal metabolism is regulated by centers in the interbrain independent of the heat center. When they injected silver nitrate solution into the posterior portion of the interbrain basal metabolism was lowered.

Neurologists now frequently see patients with parkinsonian tremor with increased metabolic rate who have had thyroidectomy with little or no benefit. I shall briefly relate some of my own experience with cases offering problems as to the parts played by head trauma, encephalitic virus, the thyroid and the hypophysis.

CASE REPORTS

CASE 1. A woman 52 years old, previously healthy, on Feb. 9, 1926, struck her head against the top of a taxicab and was dazed for a few moments. She had severe pain on the left side of the forehead and at the occiput, which kept her awake during the night. The next day she noticed a tremor in the right arm and a few days later, in the jaw and right leg. The pain subsided in a few weeks but the tremor persisted. Before the accident her weight was 229 pounds. When first seen by me on July 15, 1926, her weight was 179 pounds. There was a constant tremor of parkinsonian type in the right arm and much of the time a similar tremor in the right leg and jaw. This tremor was suppressed by voluntary movement. She did not swing the right arm in walking. There was no visible thyroid enlargement and the basal metabolic rate was +1. The pulse rate during three days of observation at this time ranged from 80 to 110. The condition remained about the same for the next three months, during which time she had frequent and profuse nose-bleed. In November the pulse rate became more rapid and on December 3 the basal metabolic rate was +73 and four days later after continuous rest in bed it was +48. The pulse rate ranged from 80 to 130 and was usually above 100. After a few weeks on Lugol's solution the basal rate was +1 on January 27, 1927, but on May 21 it was +38, at which time the weight was 161 pounds. During a stay of 12 days in the hospital at this time the pulse rate was usually below 100. The tremor was less marked and involved chiefly the lower jaw. No further examination has been made, but in the latter part of May, 1930, the patient states that she still has tremor, but is able to work in a store and that she has had no more basal tests. I gave the opinion that the head injury had brought on the paralysis agitans syndrome. If this is true it may also be true that changes in vegetative brain centers later brought on the hyperthyroid syndrome.

CASE 2. A married woman 28 years old, mother of two children, was seen on March 11, 1929, on account of a parkinsonian tremor of the left hand which had been present for a year. There was also at times a tremor of slower rate in the left foot. During the preceding three years her weight had gradually increased from 140 to 197 pounds. There was no history of an acute attack of encephalitis. During the following months she began to lose weight and the pulse rate became more rapid. On April 22, her weight was 176 pounds, basal rate +38. The spinal fluid was normal. The serum calcium was 10.9. The tremor was partially controlled by hyoscin. On November 5 the weight was 159 pounds, basal rate +20. Lugol's solution was given for several weeks, but on February 27, 1930, the weight was 143 pounds and the basal rate +35. The

pulse rate became more rapid. On April 22, her weight was 176 pounds, basal rate +38. Since then the patient has been taking hyoscin, has gained a little in weight and improved in strength. The tremor is less marked but remains typically parkinsonian. The thyroid gland is not enlarged. It is thought that this is a case of chronic epidemic encephalitis and that the obesity, tremor, and subsequent loss in weight and increased metabolic rate are the results of disease involving brain centers rather than endocrine glands.

If time permitted I might cite numerous cases of true paralysis agitans with increased metabolic rate and with and without thyroid enlargement and in which thyroidectomy has been of dubious value. I might tell of young encephalitic patients with combinations of many kinds. Thus, a man of 23 years, who gave a history of an acute illness with diplopia at 18, became obese, drowsy, had upward spasms of the eyeballs and athetoid movements of the left hand. His weight was 197 pounds, blood pressure 164, pulse rate 70, and basal metabolism +26.

Another interesting syndrome with similar problems is symmetrical lipomatosis, which may appear or be suddenly aggravated in connection with mental and nervous phenomena. This condition is undoubtedly related to, in fact may merge into, the so-called adiposis dolorosa, which, however, is itself scarcely a clinical entity.

CASE 3. A woman, 52 years old, whose aunt had lipomas, was seen in December, 1929, during a depressive, confusional psychosis, without signs of organic brain disease. She had had multiple lipomas for years, but during the psychosis they had rapidly increased in number, size and tension. They were located about the neck, upper back and arms. The basal metabolism was —13. However, she grew worse on thyroid and developed attacks of rapid breathing. Curiously enough, when her physician, Dr. Leslie Rutherford of Peoria, substituted Lugol's solution, a rapid improvement in mental symptoms and reduction in the size of the lipomas set in.

CASE 4. A professional man of 30 years, first seen last February through the courtesy of Dr. Woodyatt, had been gaining weight for four years, complained of thirst and increased diuresis for four months, during which time he also showed a mild mental disturbance, especially in the line of being talkative and hailing strangers on the street. Last December symmetrical lumps appeared over the zygomas and on the neck. The skin over them appeared edematous and red and the patient complained that these areas felt very hot. Last January sugar was found in the urine and glycosuria still persists. It can be controlled by insulin but the polyuria remains and requires pituitrin. Leucocytosis is persistent, the latest count, on June 18th, being 19,300. One of the lumps on the neck was excised and was found to consist only of fat. Visual fields, sella roentgenograms and basal metabolic rate were normal. Ataxia of the left arm was present early and followed by slight, but definite, weakness of the left arm. Otherwise motor and sensory condition and reflexes have been normal. To my mind a case of this kind is better explained by an encephalitic lesion in the interbrain, affecting vegetative centers, or by a functional disorder of these centers, than by any primary affection of the hypophysis or other endocrines.

We might discuss the endocrine features of muscular dystrophy, generalized neurofibromatosis and many other obscure conditions, but I do not wish to waste your time with speculations. For the same reason I shall dismiss the huge field of the relationship of endocrinology to psychiatry with the statement that there are so many unknown factors in both of these sciences that few conclusions can be drawn. Study of endocrine conditions in definite psychoses, of psychic conditions in definitely demonstrated endocrine disorders, and of psychic reactions to administration of endocrine

preparations containing known hormones are three of the roads which may lead us to more knowledge.

Once more I wish to express my regret that, unlike my predecessors, I cannot give you any account of research work. I can only make a plea for continued cooperation between workers in the fields of endocrinology and neurology and express the hope and conviction that future research on the vegetative nervous system, and particularly on the intracranial part of it, will bring significant results.

BIBLIOGRAPHY

1. Stern, F.: Die epidemische Encephalitis, 2nd ed. Berlin, 1928, p. 105.
2. Stern: Med. Klin. **18**: 864. 1922.
3. John, E.: Deutsch. Ztschr. f. Nervenheilk. **80**: 299. 1924.
4. Wimmer, A.: Chronic Epidemic Encephalitis, London, 1924, p. 29.
5. Riese, W.: Klin. Wchnschr. **7**: 1954. 1928.
6. Naccarati, S.: J. Nerv. & Ment. Dis. **63**: 219. 1926.
7. Steinhaus: Paper read before Chicago Soc. of Int. Med., May, 1930.
8. Gräfe, E. and E. Grünthal: Klin. Wchnschr. **8**: 1013. 1929.

THE ACTION OF PITUITRIN, PITRESSIN AND PITOCIN ON THE BLOOD PHOSPHATIDES

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The posterior pituitary hormone, pituitrin, exerts some characteristic effects on fat-metabolism and seems to be an important factor in the consumption and distribution of body fat. These facts were demonstrated experimentally for the first time in 1925 by Coope and Chamberlain (6), who found a considerable accumulation of fatty acids within the liver under the influence of pituitrin and by Raab's (14) studies on the changes of blood fat and blood acetone bodies through various hormone preparations. Pituitrin was the only one that produced a marked and comparatively long lasting action on the blood fat level—a regular decrease during several hours. For obtaining this effect in fasting dogs large doses of pituitrin are needed if injected subcutaneously, while the same effect can be produced by very small doses (0.18 cc.) if injected into the third ventricle of the brain. The pituitrin effect is abolished by destruction of the tuber cinereum at the base of the mesencephalon, by paralyzing the mesencephalic centers with drugs (acetyl-salicylic acid, etc.), by transection of the cervical spinal cord, by section of the splanchnic and by paralyzing the sympathetic nervous endings with ergotamin. Hence pituitrin appears to act on the fat metabolism through a nervous path starting in the midbrain and ending with the splanchnics. The fat disappearing from the blood stream is accumulated and probably subsequently destroyed in the liver. (Clinical cases of both hypophyseal and cerebral type of obesity may, therefore, probably be considered as due to a disturbance of the function of the so-called "hypophysis-mesencephalon system" as far as its stimulating effect on fat destruction is concerned.) Raab's (14) first experiments were based on the determination of the total petroleum-ether fraction (containing neutral fat plus free cholesterol). Later on Blix and Ohlin (1) and Raab (14) stated that the effect of pituitrin results merely in a decrease of neutral fat while the cholesterol remains practically unaltered. The acetone bodies of the blood show a slight fall (Raab, 14). The findings of Coope and Chamberlain (6) (increased fat absorption by the liver), although not confirmed by van Dyke (7), have been corroborated recently by Oshima (13) and by Steppuhn, Timofejewa and Ljubowzowa (15). The latter found also a corresponding loss of fat in the peripheral tissues but do not believe in a destruction of fat within the liver because the amounts of fat in the liver, as well as in the tissues, return again towards the normal after some time. Yet the total fat content of the body seems to be diminished by pituitrin.

*Research Fellow of the Rockefeller Foundation.

Blix and Ohlin (1) observed that pituitrin decreased the blood phosphatides even more than neutral fat and emphasize the important rôle of the phosphatides in the intermediary metabolism of fat which has also been pointed out by Bloor (3), Jost (9) and others.

Recently there have been carried out most interesting experiments on the effect of total sympathectomy by Cannon and his collaborators (4). The close relationship between the action of pituitrin on blood fat and the sympathetic nervous system shown by Raab led Dr. Cannon to suggest experiments with pituitrin on sympathectomized dogs. Two of his operated animals were kindly placed at my disposal. Because of Blix and Ohlin's statement of a particularly strong action of pituitrin on the blood phosphatides I decided to use this effect as a test and to employ for the determination of lipoid-phosphorus in the blood (alcohol-ether extract after Bloor) the method of Fiske and Subba Row (8), the accuracy of which has been confirmed by various authors.

Futhermore, it seemed of some interest to examine the two pituitrin constituents, pitressin and pitocin, which have been isolated lately by Kamm and his collaborators (10).

All experiments have been made on dogs (8 to 20 kgm.) fasting for approximately sixteen hours. No food or water was given during the experiments. Blood samples of 2.5 cc. were taken from a hind leg vein. Pituitrin, pitocin and pitressin (all Parke, Davis & Co.) were injected subcutaneously. Except for stimulation of bowel movements there was not observed any conspicuous alteration of the animal's general behavior after the injections. The doses given varied between 6 and 12 cc. (mostly 12cc.). In their specific activity on blood pressure and tone of the uterus 1 cc. pitressin corresponds to 2cc. of pituitrin and 1cc. pitocin corresponds to 1 cc. of pituitrin (personal information by Dr. Kamm).

RESULTS

(a.) *Control experiments* (fasting): The lipoid phosphorus showed considerable irregularities, rises and falls varying in amounts from +21.8 to —13.7 per cent of the initial figure (on an average from +6.2 to —3.9 per cent). See Table I.

(b.) *Pituitrin:* Doses of on an average 21 cc. (injected at once) caused in all of ten experiments a moderate drop of the lipoid phosphorus varying in degree from —4.2 to —29.1 per cent (on an average —14.6 per cent). One single rise of 1.6 per cent above the initial level in the third hour can be considered as insignificant. See Table II.

(c.) *Pituitrin in sympathectomized dogs:* The effect was not uniform. There occurred rises up to +13.8 per cent, while the decreases attained a maximum of only —15.6 per cent (on an average —6.7 per cent). See Table III.

TABLE I

CONTROL EXPERIMENTS (FASTING DOGS)

Body Weight in kgm.	Blood Lipoid Phosphorus (in mgm. %)						Maximal Differences (within 12 hours)	
	Time in Hours							
	0	3	6	9	12	24	+	−
14	14.6	14.1	13.8	14.3	13.8	**14.6**	....	5.4%
20	12.1	10.5	11.9	12.2	10.8	**11.3**	....	13.2%
20	13.4	13.0	13.0	14.8	15.2	**15.5**	13.0%	3.3%
20	13.0	13.5	12.3	12.9	11.2	**11.3**	3.4%	13.7%
14	14.4	14.3	14.2	14.4	....	**14.2**	0.3%	1.0%
14	11.0	12.4	12.5	11.7	12.0	**9.2**	13.5%	....
20	11.0	9.9	10.3	....	10.7	**10.5**	....	9.9%
9	11.9	10.4	12.0	14.5	14.2	**12.0**	21.8%	12.2%
17	13.0	12.1	13.2	12.7	12.8	**12.6**	1.1%	6.8%
12	13.0	12.2	14.2	14.2	13.0	**13.1**	9.2%	6.1%
Average:	12.7	12.2	12.7	13.5	12.6	**12.4**	6.2%	3.9%

TABLE II

PITUITRIN IN NORMAL DOGS

Body Weight in kgm.	Pituitrin	Blood Lipoid Phosphorus (in mgm. %)						Maximal Differences (within 12 hours)	
		Time in Hours							
		0	3	6	9	12	24	+	−
14	6 cc.	11.7	11.5	10.5	10.4	10.4	**10.5**	....	11.0%
14	2x10 cc.	11.4	10.5	10.4	10.2	10.2	**10.4**	....	10.9%
8	12 cc.	12.0	9.3	10.1	9.5	9.8	**10.9**	....	22.5%
20	12 cc.	10.7	9.7	8.4	9.7	10.1	**10.1**	....	21.4%
14	12 cc.	14.3	11.5	13.7	13.6	....	**13.1**	....	19.2%
16	12 cc.	13.3	12.7	12.3	12.5	....	**13.6**	....	7.5%
20	12 cc.	13.0	13.0	11.6	12.5	11.8	**14.5**	....	11.1%
20	12 cc.	15.0	15.3	14.4	14.6	14.6	**14.6**	1.6%	4.2%
17	12 cc.	16.5	14.2	....	13.8	13.6	**16.3**	....	17.5%
12	12 cc.	12.3	12.4	8.7	12.3	10.2	**13.8**	....	29.1%
Average:		13.0	12.0	11.1	11.9	11.3	**12.8**	....	14.6%

TABLE III

Pituitrin in Sympathectomized Dogs

Body Weight in kgm.	Pituitrin	Blood Lipoid Phosphorus (in mgm. %)						Maximal Differences (within 12 hours)	
		Time in Hours							
		0	3	6	9	12	24	+	−
16	12 cc.	12.5	12.0	10.7	11.4	10.6	**10.9**	....	15.2%
10	12 cc.	10.5	11.9	11.0	11.1	11.1	**11.5**	13.8%	....
16	12 cc.	14.6	14.0	13.5	13.7	13.7	**11.9**	....	7.2%
16	12 cc.	10.8	9.8	10.7	12.2	11.6	**11.6**	12.9%	9.2%
10	12 cc.	11.1	10.5	10.0	9.7	10.2	**10.6**	....	12.1%
10	12 cc.	11.3	10.5	10.6	10.6	10.5	**10.3**	....	7.1%
17	10 cc.	12.0	10.7	11.5	11.7	11.9	**11.5**	....	11.2%
17	12 cc.	13.1	11.0	11.0	11.3	11.5	**12.5**	....	15.6%
10	12 cc.	10.8	10.6	10.6	10.3	10.7	**10.8**	....	4.6%
Average:		11.9	11.2	11.1	11.4	11.3	**11.3**	....	6.7%

TABLE IV

Pitressin in Normal Dogs

Body Weight in kgm.	Pitressin	Blood Lipoid Phosphorus (in mgm. %)						Maximal Differences (within 12 hours)	
		Time in Hours							
		0	3	6	9	12	24	+	−
14	6 cc.	11.1	10.4	10.7	....	10.5	**10.4**	....	6.2%
20	12 cc.	12.5	10.3	11.5	11.5	9.7	**10.9**	....	22.4%
17	12 cc.	14.6	14.6	15.2	15.3	14.5	**15.8**	4.7%	....
20	6 cc.	13.7	13.5	13.6	13.7	13.8	**13.8**	0.8%	1.1%
17	6 cc.	12.8	12.8	11.9	13.8	13.8	**13.5**	7.3%	7.0%
20	12 cc.	13.5	12.5	13.6	13.0	14.5	**14.7**	7.7%	7.4%
19	12 cc.	14.7	13.5	13.5	14.1	14.5	**14.2**	....	8.4%
18	12 cc.	11.6	11.5	11.3	10.8	11.1	**10.8**	....	6.8%
Average:		13.1	12.4	12.0	13.2	12.8	**13.0**	....	8.4%

(d.) *Pitressin:* There appeared no uniform effect. Rises went up to +7.7 per cent, falls down to —22.4 per cent. The average curve showed a fall to —8.0 per cent. See Table IV.

(e.) *Pitocin:* There occured both rises and falls within a range from +17.9 to —31.8 per cent. The average curve showed a fall to —9.8 per cent. See Table V.

(f.) *Egg yolk intravenously:* No marked hyperlecithinemia was observed after the injections. As early as five minutes after the end of the injection the lipoid phosphorus appears practically unchanged.

TABLE V

PITOCIN IN NORMAL DOGS

Body Weight in kgm.	Pitocin	Blood Lipoid Phosphorus (in mgm. %)						Maximal Differences (within 12 hours)	
		Time in Hours							
		0	3	6	9	12	24	+	−
14	6 cc.	12.8	12.9	15.1	....	11.5	....	17.9%	10.5%
8	12 cc.	13.3	12.5	12.4	12.7	12.9	**12.3**	....	7.1%
19	12 cc.	13.8	12.6	12.7	12.4	12.0	**13.1**	....	13.3%
16	12 cc.	13.5	12.8	14.2	14.2	12.7	**13.2**	5.2%	5.5%
21	12 cc.	12.8	12.8	11.3	12.2	11.7	**10.9**	....	11.7%
17	12 cc.	12.8	13.7	12.8	13.0	....	**13.5**	7.0%	....
17	12 cc.	13.8	13.2	13.8	13.5	13.5	**12.5**	....	3.9%
12	12 cc.	13.5	12.7	12.8	12.0	9.2	**11.1**	....	31.8%
Average:		13.2	12.9	13.1	12.8	11.9	**12.4**	....	9.8%

DISCUSSION

The effect of pituitrin in decreasing the blood lipoid phosphorus, although regularly present, was not as striking as had been expected with regard to Blix and Ohlin's (1) data concerning the blood phosphatides determined with Bang's method. This phenomenon is, therefore, not very suitable for use as a functional test, especially considering the frequent spontaneous decreases of lipoid phosphorus values even in the control experiments. In contrast the petroleum-ether fraction and neutral fat usually increase during thirty hours fasting periods (Raab, 14). The cause of this quantitative discrepancy between Blix and Ohlin's and my own findings is not quite clear. Even the possible assumption of the presence of varying phosphorus-free substances within the "phosphatide fatty acids" determined after Bang-Blix would hardly explain the large difference between a maximum drop of 80 per cent (average 53 per cent) in Blix's and a maximum drop of only 29.1 per cent (average 14.5 per cent) in my experiments, although Blix (2) himself says: "As the nature of the phospha-

tides in the blood is unknown it is clear that the calculated phosphatide value by no means may be regarded as a real expression of the quantity of phosphatides actually present. Even if the phosphorus content of the blood phosphatides should be approximately the same it is not certain that the fatty acid content is the same (in lecithin and cephalin there are two molecules of fatty acid, in sphyngomyelin probably one), and the phosphorus value thus besides tells very little about the quantity of fatty acids contained in the phosphatides." The preparation used was the same (Parke, Davis & Co.); the dosage it is true has been relatively somewhat smaller in some of my experiments, but not enough to give a satisfactory explanation. The type of previous diet as well as the species of animals may perhaps be of a certain importance for the quantitative results.

Attempts were made to produce an exogenous hyperlecithinemia for the purpose of testing the action of pituitrin on the artificially increased blood phospholipids. Oral feeding with lecithin does not produce any significant increase of the blood lipoid phosphorus (Leites, 11), while Nerking (12) supposes (without, however, giving any experimental evidence for it), a long lasting retention of lecithin if injected into the blood stream, and Bloor (3) attributes the comparatively slow disappearance of fat from the blood after intravenous injection of egg yolk (0.6 to 0.8 gm. per kgm. body weight) to a retention by the presumably circulating lecithin which forms about 30 per cent of the egg yolk lipoids. My own experiments with intravenous injection of egg yolk (0.6 to 1.0 gm. per kgm. body weight) show that the phospholipids injected in this form disappear entirely from the blood within a few minutes and that it is not possible to produce a prolonged exogenous hyperlecithinemia by this means.

A complete absence of the pituitrin effect in the sympathectomized dogs cannot be claimed with certainty, yet in contrast to normal animals there occurred rises up to +13.8 per cent and the decreases both maximum and average were smaller than in normal animals. It might be mentioned that the bilateral removal of the thoracic and abdominal sympathetic had been done about one year before. The pituitrin effect was markedly weakened if not abolished in these completely sympathectomized animals.

The least enlightening results were obtained by the pitressin and pitocin experiments. Both of them led to rises and falls of the lipoid phosphorus level, the latter being more frequent and more intense it is true. The decreases amounted to 22.4 per cent in the case of pitressin and to 31.8 per cent in the case of pitocin. It is, however, not possible to attribute the specific activity of the total pituitrin to one of the two fractions after these experiments, and it rather seems as if both of them may exert a certain influence. Determinations of their action on neutral fat will probably give clearer results.

In connection with the above mentioned facts concerning the influence of the hypophysis-mesencephalon system and of pituitrin on fat metabolism it seems justified to consider the intermediary and posterior lobe of

the pituitary as important factors in the maintenance of normal quantitative conditions of fat balance as a part of the internal body equilibrium or "homeostasis" (Cannon, 5).

SUMMARY

(a.) The findings of Blix and Ohlin (1) concerning a depressant action of pituitrin on the phosphatides of the blood are confirmed (by use of determination of the blood lipoid phosphorus), although in a quantitatively considerably smaller degree.

(b.) In sympathectomized dogs somewhat irregular results suggest that this effect is weakened if not entirely absent.

(c.) The effects of pitressin and pitocin are irregular. Yet, they suggest that both of these fractions of pituitrin exert a certain influence on the blood lipoid phosphorus similar to that of pituitrin.

(d.) There cannot be produced a marked increase of the blood lipoid phosphorus by intravenous injection of egg yolk.

I wish to express my gratitude to Professor Cannon for the permission to use his sympathectomized animals and for all facilities granted to me in his laboratory.

BIBLIOGRAPHY

1. Blix and Ohlin: Skandinav. Arch. f. Physiologie, **51**: 167. 1927.
2. Blix: Studies on Diabetic Lipemia. Lindstedts Univ. Bokhandel, Lund, 1925.
3. Bloor: J. Biol. Chem., **19**: 1. 1914, and **25**: 577. 1916.
4. Cannon, Newton, Bright, Menkin and Moore: Am. J. Physiol., **89**: 84. 1929.
5. Cannon: Physiol. Reviews, **9**: 399. 1929.
6. Coope and Chamberlain: J. Physiol., **60**: 69. 1925.
7. van Dyke: Arch. f. exper. Pathol. u. Pharmakol., **114**: 262. 1926.
8. Fisk and Subba Row: J. Biol. Chem., **66**: 375. 1925.
9. Jost: Proc. XIIIth Physiolog. Congress, Boston, 1929. Am. J. Physiol., **90**: 404. 1929.
10. Kamm, Aldrich, Grote, Rowe and Bugbee: J. Am. Chem. Soc., **50**: 573. 1928.
11. Leites: Biochem. Ztschr., **184**: 310. 1927.
12. Nerking: München. med. Wchnschr., 1909, p. 1475.
13. Oshima: Ztschr. f. die ges. exper. Med., **64**: 694. 1929.
14. Raab: Ztschr. f. die ges. exper. Med., **49**: 179, 1929; **53**: 317, 1926; **62**: 366, 1928.
15. Steppuhn, Timofejewa and Ljubowzowa: Wjestnik Endokrinologii, **3**: 81. 1929. (Russian).

STUDIES IN THE PHYSIOLOGICAL PROPERTIES OF THE GROWTH-PROMOTING EXTRACTS OF THE ANTERIOR HYPOPHYSIS*

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Evans and Long (1), in 1921, first reported remarkable overgrowth in female rats, which had been brought about by daily intraperitoneal injections of a saline emulsion of the fresh bovine anterior hypophysis. They also called attention to a peculiar effect which these emulsions had on the oestrous cycles and the ovaries of the injected animals. Oestrus occurred infrequently or was completely inhibited, and the ovaries, in many instances, were found to be enlarged. The enlargement proved to be due to the proliferation of lutein tissue in the walls of follicles, which was frequently so extensive that solid corpora lutea were formed. Ova were found enclosed within many of these corpora showing that their formation had not been preceded by true ovulation as occurs in the formation of normal corpora lutea. In young animals the onset of the first oestrus was delayed.

Further work by Evans (2) and his associates led to more efficient methods of extracting the growth-promoting principle from the gland.

Four years ago studies were begun in this laboratory on the properties and effects of these growth-stimulating extracts. Preliminary studies with extracts prepared according to the methods of Evans and his associates fully confirmed their observations on rats, a veritable gigantism resulting after several months' injection.

However, the procedure of the California workers, of preparing the extracts daily from fresh glands, proved so time-consuming and expensive that we cast about for a method of preparing sterile extracts which could be preserved. By means of a slight modification of the method of Evans, and the use of the Seitz filter, it became possible to prepare a sterile limpid extract which retained its activity for weeks if kept at freezing temperature (3).

With this readily absorbable fluid experiments previously restricted to rats were extended to dogs, a step which seemed advisable for several reasons. In the first place rats retain the ability to grow throughout life. Moreover, their bony epiphyses never completely close so that a syndrome simulating acromegaly could hardly be expected in this species. On the other hand, in the dog, in which the epiphyses do close, the production of a state resembling acromegaly in man seemed possible. Furthermore, it was highly desirable to extend the studies to canines because the use of this

*Read before the International Physiological Congress, August, 1929, Boston.

larger animal permits chemical and metabolic studies on blood and urine that are difficult or impossible in the rat.

Injections, continued for over a year in a pure-bred English bulldog (with littermate control), brought about a condition closely simulating human acromegaly (4). The experimental animal grew rapidly and developed marked acral enlargement. Many of the symptoms and signs of clinical acromegaly became apparent, including a voracious appetite, asthenia, hypotonia, sialorrhea and spontaneous lactation, as well as disproportionate enlargement of the tongue, and considerable increase in the amount, and change in the texture, of the cutaneous tissues. The injected animal never showed evidence of oestrus.

Definite skeletal overgrowth was demonstrable at postmortem (Fig. 1), and what was of even greater interest, a remarkable splanchomegaly comparable to that characterizing human acromegaly (5) was found. The whole digestive system, especially the liver, was greatly hypertrophied as

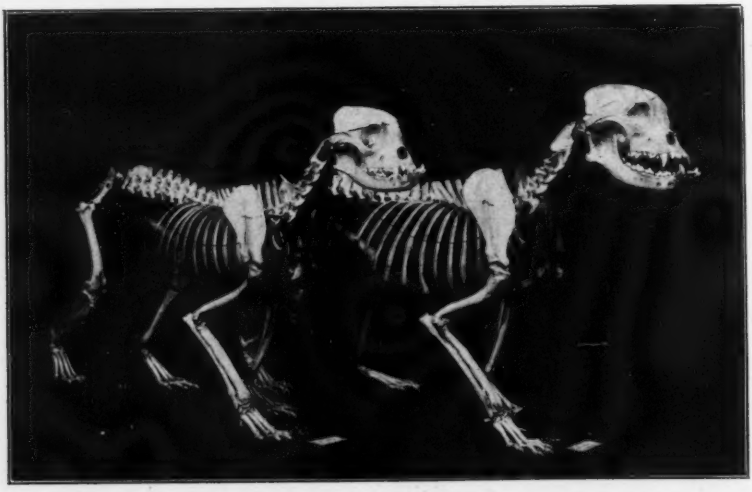

Fig. 1.—Skeleton of thorough-bred female English bulldog after 14 months of daily injection with hypophyseal growth-promoting extract. The skull of the littermate control is shown on the left for comparison.

were the thyroids, adrenals, heart, and kidneys, but the disproportion in size was greatest in the genital tract. The vagina and uterus had become greatly hypertrophied and the ovaries were four times the weight of those of the control, the increase in size of the latter organs being largely due to increase in stroma. A few large follicles and many atretic ones were seen but there were no corpora lutea.

It was perhaps unfortunate and misleading that the first prolonged experiment was made on a bulldog, an animal that might be regarded as potentially having acromegalic features. Entirely comparable and equally definite experimental overgrowth has since been produced in other animals

Fig. 2.—This mongrel male Airedale was approximately 14 months old and had not gained in weight during the six weeks of observation before injections were begun. Photograph taken after six months of daily injections when the animal had doubled in weight and marked acral enlargement was apparent. Autopsy revealed striking splanchnomegaly.

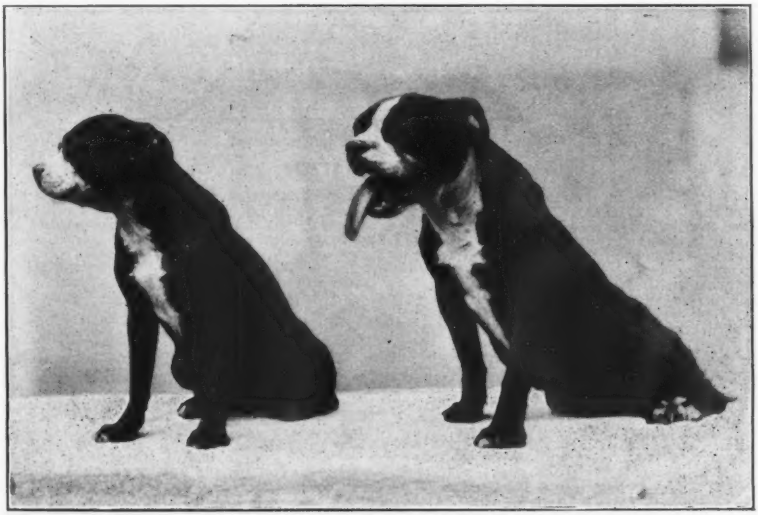

Fig. 3.—Year-old littermate Boston terriers of pedigreed stock. At the age of five months, when injections were begun, the experimental animal (right) was slightly smaller than the control.

both male and female of other breeds (Fig. 2 and 3). In males there results a loss of libido associated with a varying amount of atrophy in the testes which is sometimes extreme.*

Having obtained these pronounced effects on the growth and behavior of the animals, we proceeded to study their food and water metabolism.

STUDIES IN BLOOD CHEMISTRY

In collaboration with Dr. O. Watkins of the Department of Biochemistry (6), certain of the constituents of the blood of fasting dogs were followed after parenteral administration of the growth-promoting extracts. It was found that about twenty hours after the last feeding the non-protein nitrogen in the blood of the normal animal reaches a fasting level at which it remains practically constant. After this level is once established there

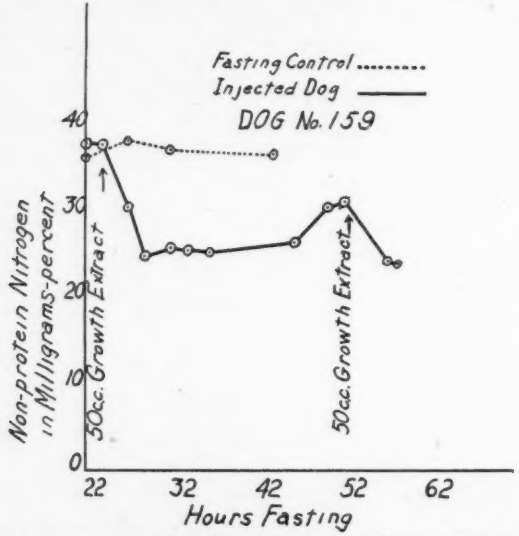

Fig. 4.—Graph showing the effect of intraperitoneal injection of growth-promoting extract upon the level of non-protein-nitrogen in the blood of a fasting dog. (The relatively constant value in a representative control experiment is shown in the dotted line for comparison.) In this experiment the injection was repeated when the non-protein-nitrogen had begun to rise again to the normal fasting level, resulting in a repetition of the effect.

is no further lowering; indeed, after prolonged fasting (weeks) the non-protein nitrogen tends to rise slightly as shown by Morgulis. Accordingly the experiments were all begun after at least twenty hours' fast and it was found that injection of the growth extracts led to a further considerable drop in the level of the fasting non-protein nitrogen, of from 20 to 30 per cent. This drop did not come immediately but only after a latent period of from three to six hours, after which the level remained low for some hours and did not rise again to the previous fasting level until the lapse of eighteen to twenty-four or more hours (Fig. 4). The fall in the non-protein

*The effects of these relatively crude growth-promoting extracts on the gonads and genital system should not be confused with the more recently described *gonad stimulating* effects of other preparations from the anterior lobe.

nitrogen was distributed among urea, amino acid, and "undetermined" nitrogen, roughly in proportion to their respective normal concentrations in normal fasting blood.

Control injections of extracts after boiling, which is known to destroy the growth principle, brought about no such response (Fig. 5). Posterior lobe extracts were also ineffective in this respect as was ox serum which had been diluted with a sodium acetate solution to the point at which the protein and sodium acetate concentrations corresponded with those in the growth extracts.

Slight changes in serum calcium and inorganic phosphorous were also observed but were not constant and they were not followed in a large

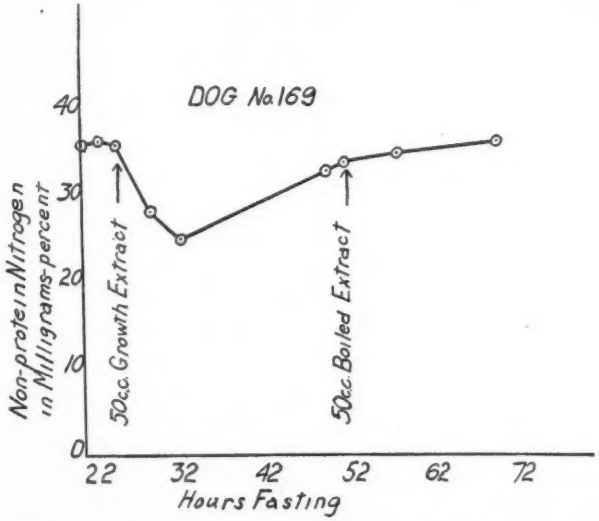

Fig. 5.—Graph showing, first, the effect of an active growth-promoting extract upon the level of non-protein-nitrogen in the fasting blood; and second, the inactivity of the same preparation after boiling. (Compare this with figure 4 in which the active preparation was repeated.)

enough series of cases for us to be certain of any real effect. There were no significant fluctuations in the blood sugar during the period of the experiments.

The disappearance of nitrogen from the blood following injection suggested that it was either excreted in the urine or was stored in the tissues. The latter supposition appeared to be supported by the rapid gain in weight of the injected animals, and especially by the splanchnomegaly which follows such treatment.

A few analyses of two hour samples of urine taken before and after injection convinced us that the two-hour excretion of nitrogen in the urine fluctuated too greatly to give reliable information on this score.

STUDIES ON THE METABOLISM OF NITROGEN PHOSPHORUS AND CALCIUM

Failure to prove the fate of the disappearing non-protein nitrogen from the blood by analysis of urine for brief periods preceding and following injection led to more prolonged balance-experiments.

In collaboration with Dr. Walter Bauer of the Massachusetts General Hospital the following observations were made. The dogs were fed a constant amount of a modification of Cowgill's synthetic diet and the elimination of nitrogen calcium and phosphorus was determined for a period preceding and another during injections of the growth-stimulating extracts. In spite of the fact that the diet, and hence the calorific intake, remained constant, analyses of urine showed that there was marked retention of nitrogen; moreover phosphorus practically disappeared from the urine. The calcium excretion in the urine on the other hand was considerably increased during the first few days following injection.

STUDIES IN GASEOUS METABOLISM

Having found that a notable retention of nitrogen follows injections of the growth-promoting substance in spite of the fact that the calorific intake remains constant, it seemed not unlikely that if this observation were correct the gaseous metabolism might compensatorily be diminished.

Preliminary determinations of the basal metabolic rate of the injected dogs showed that the rate at least was not accelerated, the figures actually indicating a diminished rate. Since Dr. Benedict's most recent and highly accurate metabolism-apparatus for rats was available in the laboratory of Dr. Hoskins and Dr. Lee, with Dr. Lee's (7) cooperation, the metabolism of four of our giant-rats was determined. In each animal the basal metabolic rate was definitely diminished, the average of the determinations for all four of the animals being 13 per cent below that of a large control series of other normal rats. In two of the giant animals the injections were omitted for three weeks during which time the animals lost some weight although they were still considerably heavier than their controls. Metabolism determinations on these animals after discontinuance of the injections showed that the rates had risen to within normal limits.

It would appear that the drop in the level of the blood non-protein nitrogen, the retention of nitrogen from the diet, and the diminished metabolic rate following injection are not incompatible findings.

STUDIES IN WATER METABOLISM

During the course of prolonged experiments on growth, it was casually observed that there was considerable diuresis following injection of some preparations of the growth-promoting extracts.

Measurement of the water intake, urine output, and specific gravity for some days before, and following injections of the extracts, showed that some

of them possessed remarkable diuretic properties (Fig. 6). A single daily injection of 25 cc. in a number of instances increased the twenty-four hour intake and output more than ten fold. One animal whose average twenty-four hour output during the control period was 700 cc., after injections were begun, excreted as much as 7300 cc. of urine in twenty-four hours and the daily elimination remained above five liters during a week period of observation. The specific gravity of the twenty-four hour specimens fell from *circa* 1040 to *circa* 1003. Moreover, the diuresis did not begin for twenty-four or more hours following the first injection and the effect per-

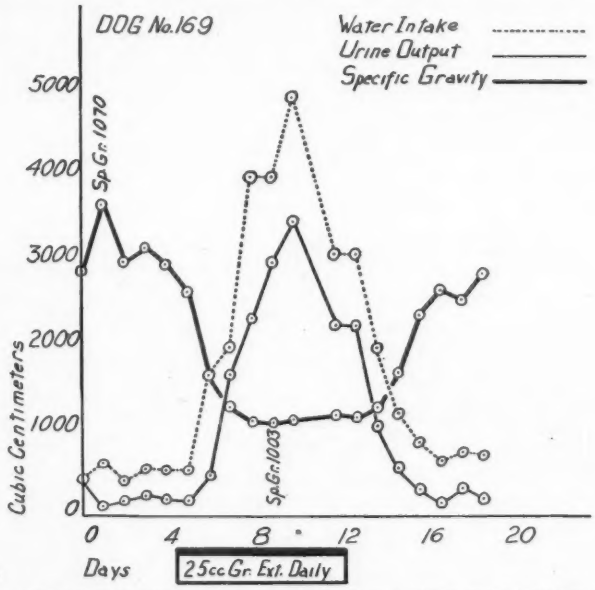

Fig. 6.—Graph showing the marked diuretic effect of a single daily injection of 25 cc. of growth-promoting extract. Not all the extracts which accelerated growth produced the diuretic effect.

sisted for two or three days following the last one. Not all of the growth extracts possess this diuretic effect, although there have been no extracts which produce diuresis which do not also stimulate growth in rats. We are not yet able to state whether growth and diuresis are due to the same substance.*

BIBLIOGRAPHY

1. Evans, H. M. and J. A. Long: Anat. Rec. **21**: 62. 1921.
2. Evans, H. M.: Harvey Lectures, Lippincott, Phila. 1924.
3. Putnam, T. J., H. M. Teel and E. B. Benedict: Am. J. Physiol. **84**: 157. 1928.
4. Putnam, T. J., E. B. Benedict and H. M. Teel: Arch. Surg. **18**: 1708. 1929.
5. Cushing, H. and L. M. Davidoff: Monogr. of the Rockefeller Inst. Med. Res. No. 22.
6. Teel, H. M. and O. Watkins: Am. J. Physiol. **89**: 662. 1929.
7. Lee, M. O., H. M. Teel and J. Gagnon: Proc. Soc. Exper. Biol. & Med. **27**: 23. 1929.

*Recently Dr. Oliver Kamm of Parke, Davis and Company has informed us that he has repeated the experiments on diuresis. He states that he has evidence which suggests that the diuresis may be due to a non-specific protein reaction, rather than a specific hypophyseal effect.

DOES THE ZONDEK PITUITARY HORMONE INFLUENCE THE GROWTH OF THE BODY?

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Director: Prof. Dr. G. P. Sakharoff
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It is beyond the least doubt that the anterior lobe of the pituitary body is the source of a hormone stimulating the growth both of the whole body and of various separate organs. Not only do the clinical observations upon dwarfism, gigantism and acromegaly support this proposition, but also the experimental studies, particularly the cessation of the growth and development of the body following ablation of the anterior lobe of the hypophysis.

For the most part attempts to provoke gigantism in animals by means of pituitary extracts have given but doubtful results. It is true, however, that Wulzen's experiments on planarian worms (1), Uhlenhuth's on axolotls (2), Long and Evans' on rats (3) and Putnam's on dogs (4) have shown the possibility of stimulating the growth of the young animals by the aid of parenteral injections of anterior pituitary substance or of its extracts. These extracts, however, were of too indefinite composition, and no opinion could be formed as to the nature and properties of their active principles.

After Zondek's discovery of the anterior pituitary hormone provoking the rapid growth and development of the sexual glands both in females and in males, many investigators, including one of us (5), showed that using the method pointed out by Zondek it is easy to obtain from the pituitary body and from the urine of the pregnant women a substance which is the "primary sexual hormone," and is capable of provoking in a very short time the full development of the sexual glands in infantile animals. We did not find, however, either in literature or in our own experiments any evidence concerning the increase of the growth of these animals. We supposed then that it was the insufficient quantity of the hormone, as well as the short duration of the experiment, that were the causes of the absence of such an effect. For this reason we have performed a series of experiments on the white rats, using large quantities of this hormone and prolonging the experiment to 50 days.

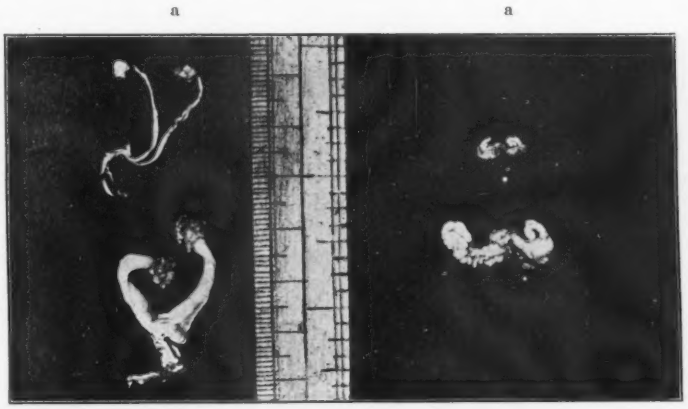
As a preparation of anterior pituitary hormone, we used the "Pituicrin A" of the State Institute of Experimental Endocrinology in Moscow; this preparation contained 20 mouse units per cubic centimeter. The experiment was performed on 24 rats. It is impossible to have such a quantity of animals belonging to one litter; so we had chosen our rats that every two or three rats and the control animal of the same sex be-

longed to the one litter (see table). All animals were kept under similar conditions of environment and nutrition. Each rat received daily 0.5 c.c. of the above mentioned preparation, i.e., 10 mouse units. The control animals received an equal quantity of physiological saline solution. The weighing was performed weekly and we started studying the vaginal secretion in females as soon as that became possible.

The experiment of 50 days' duration has given the following results:

(1) In all females which received the hormone the phenomena of the oestrous cycle appeared on the 4th to 7th day from the beginning of the experiment. None of the control females showed them during the first month.

(2) After two weeks some animals were killed and dissected. In the females which had received the hormone, uteri and ovaries were enormously increased, the average weight of the uterus being 0.45 gm., as compared with 0.065 gm. in control animals. The corresponding weight of the ovaries was 0.075 and 0.03 gm. In males it was possible to note a



Photographs of uterus and ovaries and of seminal vesicles, respectively, of control animals (above) and of injected animals (below).

considerable growth of seminal vesicles (average weight of them was 0.19 gm., while in the control males it was 0.04 gm.), while the testicles presented less difference in weight, the latter being correspondingly of 0.81 and 0.77 gm.

The accompanying photograph shows the difference in size of those organs in normal animals (a) and in animals which received the hormone (b).

(3) Notwithstanding so intense an action of the hormone on the sexual system, no difference was observed between the growth of the animals used in the experiment and of the control animals. The following table presents the corresponding numerical data:

I. First Series

Group	Animal	Litter	Weight in Grams						
			25.IX	3.X	10.X	17.X	24.X	31.X	14.X
Females	1	1	51.0	64.5	83.5	97.0	109.5	117.0	139.0
	2	1	51.0	61.5	73.5	81.0	81.5	93.0	120.0
	3	2	43.0	62.0	81.5	100.5	109.0	115.0	122.0
	4	2	40.0	58.0	75.0	87.5	101.5	115.0	146.0
Average			46.3	61.5	78.4	91.5	100.4	110.0	131.8
Control Females	5	1	50.0	63.0	81.0	91.5	101.0	108.0	129.0
	6	1	50.0	70.5	82.5	94.0	101.5	109.0	128.0
	7	2	38.0	57.5	76.5	91.0	96.0	111.0	148.0
Average			46.0	63.7	80.0	92.2	99.5	109.3	135.0
Males	8	1	50.0	70.0	90.5	98.0	118.5	137.0	172.0
	9	2	42.0	62.5	90.0	104.0	121.5	142.0	184.0
Average			46.0	66.3	90.3	101.0	120.0	139.5	178.0
Control Males	10	1	52.5	70.5	95.0	101.0	126.5	149.0	184.0
	11	2	46.0	62.5	87.0	89.5	116.0	137.0	176.0
	12	2	43.0	63.5	85.0	90.0	108.5	150.0	174.0
Average			47.2	65.5	89.0	93.5	110.0	145.3	178.0

II. Second Series

Group	Animal	Litter	Weight in Grams					
			4.X	11.X	18.X	25.X	3.XI	14.XI
Females	13	3	40.0	56.0	81.5	89.5	115.0	133.0
	14	3	38.0	57.5	75.5	Killed		
	15	3	36.0	57.5	85.5	91.0	125.0	153.0
	16	4	33.0	49.5	67.5	Killed		
	17	4	34.0	55.5	74.0	83.5	105.0	122.0
Average			36.2	55.2	76.9	88.0	115.0	136.5
Control Females	18	3	38.5	56.5	71.5	Killed		
	19	4	38.0	55.0	75.0	85.0	116.0	136.0
Average			38.3	55.8	73.3	85.0	116.0	136.0
Males	20	3	40.0	62.5	88.5	97.5	131.0	181.0
	21	4	37.5	54.0	71.5	Killed		
	22	4	39.0	58.5	83.5	Killed		
Average			38.8	58.3	81.2	97.5	131.0	181.0
Control Males	23	3	38.0	59.0	89.0	100.5	140.0	184.0
	24	4	36.0	53.5	78.5	Killed		
Average			37.0	56.3	83.8	100.5	140.0	184.0

Graphically these relations are shown in Charts 1 and 2.

SUMMARY

In 14 young rats injections were made of Zondek's anterior lobe pituitary hormone. The control animals were injected with saline solu-

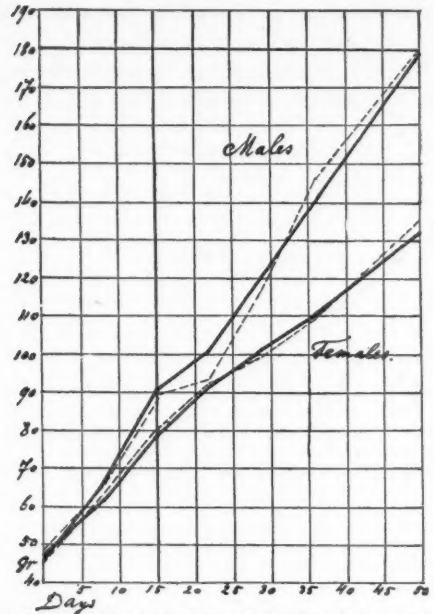


Fig. 1. Growth of control and of injected rats, series I.

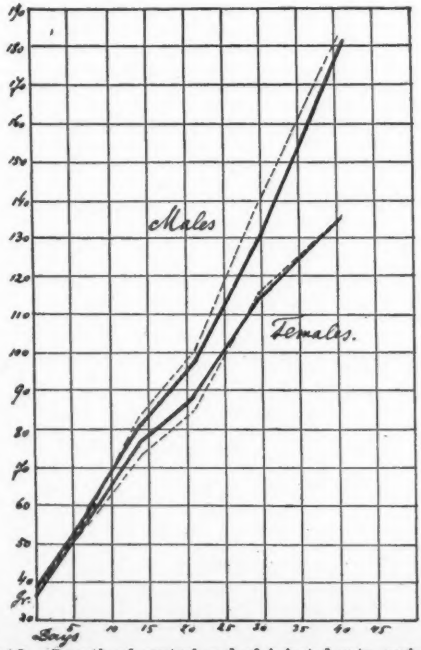


Fig. 2. Growth of control and of injected rats, series II.

tion. Although marked stimulation of the growth of the sex organs occurred, there was no influence on the growth of the young animals. It is probable that the growth-stimulating action of the pituitary body is due to another not yet isolated hormone of this organ.

BIBLIOGRAPHY

1. Wulzen: J. Biol. Chem. **25**: 625. 1916.
2. Uhlenhuth: Proc. Soc. Exper. Biol. & Med. **18**: 11. 1920.
3. Evans and Long: Anat. Rec. **21**: 62. 1921; and **23**: 19. 1922.
4. Putnam, Teel and Benedict: Am. J. Physiol. **84**: 157. 1927.
5. Botchkareff: Klin. Wchnschr. **8**: 1718. 1929.

THE EFFECT OF INTRAPERITONEAL INJECTION OF POTASSIUM IODIDE ON THE PROLIFERATIVE ACTIVITY OF THE THYROID GLAND IN RATS

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Loeb (1) has shown that oral or intraperitoneal administration of potassium iodide to guinea pigs does not prevent the compensatory hypertrophy which occurs after extirpation of the greater part of the thyroid gland. Gray and Loeb (9), Rabinovitch (2), McCordock (7), and Silberberg (3) have subsequently observed that the administration of potassium iodide orally or by intraperitoneal injections to normal guinea pigs for a certain length of time results in a very pronounced increase in the mitotic proliferation of the thyroid epithelium. It also leads to a slight increase in the size of the epithelium, to a slight softening of the colloid and to a marked increase in the number of phagocytes within the colloid. Marine (4) on the other hand maintains that the intraperitoneal injection of KI to guinea pigs previously subjected to partial thyroidectomy always prevents the onset of compensatory hypertrophy. Des Lignéris (5) had previously found that feeding KI in dogs causes an increase in the amount and hardness of colloid.

Administration of KI in Graves' disease during a short period of time causes, in many cases, an increase in the amount of colloid and a flattening of the epithelium, which may, perhaps, be the result of pressure exerted by the colloid. On the other hand, KI can also exert a stimulating effect on the thyroid gland in man; it can transform a resting colloid goiter into toxic goiter or into a condition corresponding to Graves' disease.

The experiments referred to above, in which a stimulating effect of KI was observed, were carried out in guinea pigs. It was of interest to study the effect of potassum iodide in another species with the same methods which had been used in the case of the guinea pig. We selected for this purpose the white rat. In previous experiments Loeb and Bassett (8) have already observed that extracts of anterior pituitary glands of cattle which are very active when administered to guinea pigs, are much less active in the rat. These experiments indicated that in the latter species the thyroid gland may be less responsive to stimulating agencies than it is in the guinea pig.

In this investigation three sets of rats weighing between 100 and 155 grams, were used. The rats of the first set received intraperitoneal injections daily of 0.005 gm. of potassium iodide dissolved in 0.5 cc. of sterile distilled water; the animals of the second set were injected with

0.025 gm. daily. The third set serving as controls, did not receive any injections of potassium iodide. The injections were given to different groups of animals daily for periods of 10, 15, 20, or 30 days respectively; at the end of each of these periods the thyroids were removed and studied according to the method used by Loeb, Gray and Rabinovitch (6).

COUNTS OF MITOSES

Control Animals: The number of mitoses found in the control animals varied between 0 and 1538, the average being 208 (Table I). If we discard rat 34, having an unusually high count of 1538 mitoses, the average number of mitoses per gland would be 106. By discarding rat 1 showing no mitoses at all and rat 34 with 1538 mitoses, the average falls to 114.

TABLE I
CONTROL RATS

Rat No.	*No. Mitoses per Gland	Sex	Original Weight in gms.	Final Weight in gms.	Loss or Gain Weight gms.
1	0	F	—	85	—
6	20	F	—	140	—
7	38	F	125	135	+10
10	40	M	130	155	+25
11	60	F	140	165	+25
18	219	F	130	135	+ 5
19	60	M	115	125	+10
26	156	M	120	115	— 5
27	342	M	100	120	+20
34	1538	M	—	—	—
35	80	M	—	—	—
36	100	M	—	—	—
37	139	M	—	—	—
38	120	M	—	—	—
Average	114	—	123	131	+ 8

*Both lobes, excluding the isthmus.

Animals Receiving Intraperitoneal Injections of KI for Ten Days: Animals that were given intraperitoneal injections of KI for a period of ten days neither showed a noticeable increase nor a decrease in the number of mitoses. There was no marked difference in the animals receiving the larger dose (0.025 gm.), and the ones receiving the smaller dose (0.005 gm.); the average count in the former being 140 and in the latter 119 mitoses.

Animals Injected with KI for Fifteen Days: This group does not show any striking variations either from the controls or from the ten-day group. The average number of mitoses in this group, for the animals receiving small doses of KI was 193, and for those receiving large doses it was 110. The apparent difference between these two groups is not very great and can be considered within the limits of experimental variation.

Animals Injected with KI for Twenty Days: In this group the average number of mitoses for all animals was 128; for the rats receiving the small dose the average was 53, and for those receiving the large dose it was 204. Again there is no appreciable variation in the number of mitoses from the controls.

Animals Injected with KI for Thirty Days: The average number of mitoses in this group for the animals injected with the small dose was 168 and for those receiving the large dose was 123. No striking deviation from the controls or from the other groups is seen.

It can therefore be stated that in the rat the intraperitoneal injection of KI does not have any marked effect on the proliferative activity of the thyroid gland, as judged from the number of mitoses found in this organ. It causes neither a decrease nor an increase. The number of mitoses found in each animal receiving intraperitoneal injections of KI is shown in Table II.

TABLE II

RATS RECEIVING INTRAPERITONEAL INJECTIONS OF KI

Rat No.	*No. of Mitoses per Gland	Sex	Original Weight in gms.	Final Weight in gms.	Loss or Gain in Weight gms.	†Small or Large Dose	No. of Days Injected
2	0	M	125	130	+ 5	L	10
3	38	F	155	150	— 5	L	10
8	383	F	145	135	—10	L	10
4	154	M	130	150	+20	S	10
5	40	M	130	130	0	S	10
9	162	F	145	140	— 5	S	10
12	338	M	125	135	+10	S	15
14	181	M	125	130	+ 5	S	15
15	60	M	130	150	+20	S	15
13	150	M	115	110	— 5	L	15
16	101	F	135	135	0	L	15
17	78	F	125	105	—20	L	15
21	79	M	110	125	+15	S	20
22	40	M	110	115	+ 5	S	20
25	40	M	120	125	+ 5	S	20
20	453	M	115	130	+15	L	20
23	20	M	110	100	—10	L	20
24	140	F	110	145	+35	L	20
29	220	M	115	110	— 5	S	30
31	109	M	105	110	+ 5	S	30
33	176	M	110	135	+25	S	30
28	140	M	130	125	— 5	L	30
30	210	M	115	110	— 5	L	30
32	20	M	125	130	+ 5	L	30
Average	139	—	123	127	+ 4	—	—

*Both lobes, excluding the isthmus.
†Small dose =0.005 gm. Large dose =0.025 gm.

STRUCTURAL CHANGES IN ACINI, EPITHELIUM AND COLLOID

In the control animals the acini are regular and usually small to medium in size, although occasionally they may be somewhat larger. They are lined with cuboidal epithelium and filled with solid, intensely staining, slightly retracted colloid. Sometimes vacuoles are present in the peripheral parts of the colloid. The number of phagocytes in the colloid in the lumen of the acini is variable. In some acini no phagocytes are seen, in others one may see a few phagocytes. The histological character of the thyroid in rats injected with potassium iodide does not differ materially from that seen in the controls. The size of the alveoli is approximately the same in the two groups. The epithelium in general is cuboidal but in places it may show a tendency towards a columnar shape. The colloid does not differ to any appreciable degree from that found in the controls, although occasionally it may show signs of softening processes in the glands of the animals receiving KI. The number of phagocytes does not differ noticeably in the two groups. In this connection it may be stated that on the whole the acinar epithelium of the thyroid in the rat is somewhat higher than in the guinea pig.

There are thus no decided differences in the microscopic appearance of the thyroid glands of the rats injected with KI and of the controls. But in individual cases considerable variations are present. In some animals the colloid may be of medium consistency while in others it may be hard. The average height of the acinus cells shows some variations, but in this respect also there is no consistent difference between the two groups.

The microscopic structure of the rat thyroid is somewhat different from that of the guinea pig. The three zones of different sized acini as described by Loeb and McCordock in the guinea pig thyroid are not present in case of the rat. In the latter animal the acini are usually somewhat larger in the periphery than in the center. The colloid is also more often retracted from the walls of the peripheral acini than from the central ones.

Control rat No. 34 needs especial mention for the reason that the thyroid gland of this animal showed 1538 mitoses, which is an exceptionally large number. Most of these mitoses were in the prophase or metaphase stage. No explanation for this unusually high proliferative activity seems to be available.

DISCUSSION

In contrast to the definite and large increase in the proliferative activity of the thyroid gland which takes place in guinea pigs receiving potassium iodide orally or intraperitoneally, we find no marked change in the number of mitoses in the thyroid gland of rats as a result of intraperitoneal injections of KI. There is no noticeable difference in the number of mitoses in the thyroid gland of the rats receiving KI injections for 10, 15, 20, or 30 days and in the controls. Neither do variations in the dose of KI given seem to cause here any change in the proliferative activity of the thyroid gland. The average weight of these animals was 0.125 kgm.

The doses of KI given were 0.005 gm. and 0.025 gm. in the two groups respectively. In other words, these rats received each day 0.04 gm. and 0.2 gm. KI dose per kilogram of body weight, which is equivalent to 2.8 gm. and 14.0 grams respectively per kilogram of body weight in an average man weighing 70 kgms. Even the smaller of these doses is somewhat larger than the usual dose of this drug given in man, while the larger dose would be excessive in case of man. If KI had any effect on the mitotic activity of thyroid gland in the rat it would have become noticeable with these doses. We may then conclude that in the rat potassium iodide has apparently no effect on the proliferative activity of the thyroid gland. The average number of mitoses in the rat generally is smaller than in the guinea pig. This may be due to the smaller size of the thyroid gland of this animal; but, as stated above, there are indications that the thyroid gland in the rat is more inert to various stimuli than the thyroid gland in the guinea pig. Thus Loeb and Bassett found that while extracts of anterior pituitary substance cause a very pronounced hypertrophy and hyperplasia in the thyroid gland of the guinea pig they have very little effect on the structure of the rat thyroid.

The gain or loss in body weight in the individual rats during the course of these experiments does not correspond to the increase or decrease in the number of mitoses in the thyroid gland, neither does the sex of the animals seem to be a factor in the increase or decrease of the mitotic activity of this organ.

SUMMARY AND CONCLUSION

The intraperitoneal injection in daily doses of 0.005 gm. and 0.025 gm. of KI in rats for periods of 10, 15, 20, and 30 days does not cause any appreciable change in the proliferative activity of the thyroid gland, neither does it produce any noticeable change in the structure or character of the colloid of this organ.

The average number of mitoses in the normal thyroid gland of rats is slightly lower than in guinea pigs.

The effect of administration of KI in the rat is therefore different from that observed in the guinea pig. There is some indication that, in general, the thyroid gland of the rat is less responsive than the thyroid gland of the guinea pig to various kinds of stimulation.

The author is indebted to Professor Leo Loeb of Washington University, St. Louis, for advice and assistance during this study at the Marine Biological Laboratory, Woods Hole, Massachusetts.

BIBLIOGRAPHY

1. Loeb, L.: Am. J. Path. **2**: 19. 1926.
2. Rabinovitch, J.: Am. J. Path. **5**: 91. 1929.
3. Silberberg, M.: Proc. Soc. Exper. Biol. & Med. **27**: 166. 1929.
4. Marine, D.: Arch. Path. and Lab. Med. **2**: 829. 1926.
5. Des Lignéris, M.: Experimentelle Untersuchüngen über d. Wirkung d. Jods auf d. Hundeschilddrüse, sowie über d. Hyperplasie dieser Drüse. Inaug. Diss. Bern. 1907.
6. Rabinovitch, J.: Am. J. Path. **4**: 601. 1928.
7. McCordock, H. A.: Am. J. Path. **5**: 171. 1929.
8. Loeb, L. and R. B. Bassett: Proc. Soc. Exper. Biol. & Med. **27**: 490. 1930.
9. Gray, S. H. and L. Loeb: Am. J. Path. **4**: 257. 1928.

THE RESULTS OF ORAL ADMINISTRATION OF AMNIOTIN TO MONKEYS*

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In previous experimental work we showed that when amniotin is administered by the vaginal route 2.5 times as much was necessary as when injected subcutaneously to produce an artificial sex cycle. This ratio was found to be the same in spayed rats and in ovariectomized monkeys.

Until the present time no satisfactory evidence has been given to show whether or not the follicular hormone is active when given by mouth. Many have thought that the hormone was destroyed by the digestive enzymes. Hannan claims that he obtained an estrus reaction in spayed rats when he administered 100 times the ordinary dosage.

We administered amniotin by stomach tube to the ovariectomized monkeys (Macacus rhesus) in our colony. After some preliminary difficult in getting the stomach tube inserted no trouble was experienced. The amniotin was administered once a day for five consecutive days. All monkeys used had been under observation for months. All were completely ovariectomized. The ordinary commercial preparation of amniotin and special solutions of the hormone in alcohol and glycerin were used. No difference was noted in either the types of reaction nor the amounts necessary. Vaginal spreads were taken daily and observations made of the condition of the sexual skin.

In a preliminary group of 20 monkeys, dosages varying from 700 Allen-Doisy units up to 4200 Allen-Doisy units were administered by stomach tube. These were special alcohol glycerin solutions of amniotin. In all cases menstruation was established.

TABLE I

Amniotin Used—P 520—Experimental material—Oily substance dissolved in 50% glycerin and 50% alcohol.

Five doses were given, 1 daily for 5 consecutive days by stomach tube.

Monkey No.	Dates of Feeding	Allen-Doisy Units	Duration of Epithelial Growth, Days	Duration of Menses, Days	Time Between Feeding and Menses, Days
1	2/10/30 to 2/14/30	700	11	5	14
5	2/10/30 to 2/14/30	700	9	4	16
7	2/10/30 to 2/14/30	700	11	7	15
12	2/10/30 to 2/14/30	700	15	9	22
19	2/10/30 to 2/14/30	700	9	2	18
21	2/10/30 to 2/12/30	840	7	4	15
23	2/10/30 to 2/14/30	1400	9	3	14
24	2/10/30 to 2/14/30	1400	8	6	14

*Read before The Association for the Study of Internal Secretions, Detroit, Michigan, June 23, 1930.

TABLE I—Continued

Monkey No.	Dates of Feeding	Allen-Doisy Units	Duration of Epithelial Growth, Days	Duration of Menses, Days	Time Between Feeding and Menses, Days
27	2/10/30 to 2/14/30	1400	7	5	12
28	2/10/30 to 2/14/30	1400	9	6	14
30	2/10/30 to 2/14/30	2800	6	9	10
31	2/10/30 to 2/14/30	2800	6	3	14
33	2/10/30 to 2/14/30	2800	11	6	18
34	2/10/30 to 2/14/30	2800	15	7	19
35	2/10/30 to 2/14/30	2800	11	7	17
36	2/10/30 to 2/14/30	4200	9	5	14
37	2/10/30 to 2/14/30	4200	11	5	15
38	2/10/30 to 2/14/30	4200	8	5	15
39	2/10/30 to 2/14/30	4200	13	7	18
40	2/10/30 to 2/14/30	4200	8	5	14

Average Duration of Menses—5.5 Days.

Average Duration of Epithelial Growth—9.6 Days.

Average Number of Days between 1st injection and appearance of menstruation—15.4 Days. The longest flow lasted 9 days—the shortest 2 days. There was no correlation between the dosage given and the duration of the menstruation. Similarly there was no difference in the length of time between the administration of the amniotin and the onset of bleeding. It is worth noting that such massive doses as 4200 Allen-Doisy units to these small animals produced no toxic effects nor secondary reactions.

A second group of 15 monkeys were given orally, dosages varying from 100 to 800 Allen-Doisy units. The same preparation as above was used—a glycerin alcohol solution. Four animals on 100 units and three on 200 units did not respond. Four on 400 and four on 800 units gave a menstrual reaction. As in the previous group the duration of the menstrual flow showed no relation to the dosage. The average length of menstruation was 4.9 days.

TABLE II

Amniotin Used—P 520—Experimental material—Oily substance dissolved in 50% glycerin and 50% alcohol.

Five doses were given, 1 daily for 5 consecutive days by stomach tube.

Monkey No.	Dates of Feeding	Allen-Doisy Units	Duration of Epithelial Growth, Days	Duration of Menses, Days	Time Between Feeding and Menses, Days
30	3/17/30 to 3/21/30	100	0	0	0
31	3/17/30 to 3/21/30	100	0	0	0
33	3/17/30 to 3/21/30	100	0	0	0
34	3/17/30 to 3/21/30	100	0	0	0
35	3/17/30 to 3/21/30	200	0	0	0
36	3/17/30 to 3/21/30	200	0	0	0
38	3/17/30 to 3/21/30	200	0	0	0
40	3/17/30 to 3/21/30	400	8	6	18
53	3/17/30 to 3/21/30	400	5	8	14
54	3/17/30 to 3/21/30	400	2	1	15
55	3/17/30 to 3/21/30	400	4	8	12
60	3/17/30 to 3/21/30	800	6	5	18
64	3/17/30 to 3/21/30	800	5	2	14
65	3/17/30 to 3/21/30	800	6	4	16
67	3/17/30 to 3/21/30	800	3	5	12

Average Duration of Menses—4.4 Days.

Average Duration of Epithelial Growth—4.9 Days.

Average Number of Days between 1st injection and appearance of menstruation—14.4 Days.

About 10 days after menstruation had ceased these monkeys were divided again into two groups. The ordinary commercial Amniotin was given to one group by injection and to the second group by stomach tube.

Thirteen monkeys were injected twice a day for 6 days. The total dosage varied from 25 to 150 Allen-Doisy units. One animal out of two menstruated on 75 units and the four on 100 and 150 units. In no case was menstruation obtained with less than 75 units.

TABLE III

Amniotin Used—P 568—Commercial Stock Preparation.
Two injections daily for 6 consecutive days.

Monkey No.	Dates of Feeding	Allen-Doisy Units	Duration of Epithelial Growth, Days	Duration of Menses, Days	Time Between Injection and Menses, Days
2	4/21/30 to 4/26/30	25	3	0	0
5	4/21/30 to 4/26/30	25	2	0	0
7	4/21/30 to 4/26/30	40	6	0	0
12	4/21/30 to 4/26/30	40	6	0	0
19	4/21/30 to 4/26/30	50	6	0	0
21	4/21/30 to 4/26/30	50	6	0	0
27	4/21/30 to 4/26/30	50	5	0	0
30	4/21/30 to 4/26/30	75	1	0	0
31	4/21/30 to 4/26/30	75	13	2	0
33	4/21/30 to 4/26/30	100	8	4	18
34	4/21/30 to 4/26/30	100	7	2	25
35	4/21/30 to 4/26/30	150	8	2	21
36	4/21/30 to 4/26/30	150	10	3	15

Sixteen monkeys were given the same stock solution by stomach tube. This was given once a day for five days. The dosages varied from 100-500 Allen Doisy units. None of the eleven animals on 100, 150, 200 or 300 units menstruated. Of the remaining five all gave a menstrual reaction.

TABLE IV

Amniotin Used—P 568—Commercial Stock Preparation.
Given by stomach tube once daily for 5 consecutive days.

Monkey No.	Dates of Feeding	Allen-Doisy Units	Duration of Epithelial Growth, Days	Duration of Menses, Days	Time Between Feeding and Menses, Days
38	4/21/30 to 4/25/30	100	2	0	0
40	4/21/30 to 4/25/30	100	1	0	0
53	4/21/30 to 4/25/30	150	0	0	0
60	4/21/30 to 4/25/30	150	0	0	0
64	4/21/30 to 4/25/30	150	2	0	0
65	4/21/30 to 4/25/30	200	0	0	0
67	4/21/30 to 4/25/30	200	0	0	0
68	4/21/30 to 4/25/30	200	2	0	0
69	4/21/30 to 4/25/30	300	2	0	0
70	4/21/30 to 4/25/30	300	2	0	0
71	4/21/30 to 4/25/30	300	2	0	0
72	4/21/30 to 4/25/30	400	4	2	22
73	4/21/30 to 4/25/30	400	3	2	16
75	4/21/30 to 4/25/30	400	4	2	15
76	4/21/30 to 4/25/30	500	6	7	10
77	4/21/30 to 4/25/30	500	5	3	22

This was again checked by taking another commercial lot of amniotin. Two groups were given this by injection and by stomach tube.

In the 10 monkeys injected, 3 at 68 units and 3 at 90 units, gave a menstrual reaction. The remainder at 30 and 45 units failed to respond.

TABLE V

Amniotin Used—P 607—Commercial Stock Preparation.
Injections twice daily for six consecutive days.

Monkey No.	Dates of Feeding	Allen-Doisy Units	Duration of Epithelial Growth, Days	Duration of Menses, Days	Time Between Injection and Menses, Days
36	5/24/30 to 5/29/30	30	5	0	0
34	5/24/30 to 5/29/30	30	7	0	0
31	5/24/30 to 5/29/30	45	5	0	0
30	5/24/30 to 5/29/30	45	6	0	0
27	5/24/30 to 5/29/30	68	7	3	17
21	5/24/30 to 5/29/30	68	7	3	16
19	5/24/30 to 5/29/30	68	5	3	17
7	5/24/30 to 5/29/30	90	5	6	17
5	5/24/30 to 5/29/30	90	7	4	16
2	5/24/30 to 5/29/30	90	9	4	16

Thirteen monkeys were given this preparation by stomach tube in dosages from 90 to 225 Allen-Doisy units. At 225, two out of four menstruated. Below that dosage only negative results were obtained.

TABLE VI

Amniotin Used—P 607—Commercial Stock Preparation.
Fed once daily for 5 consecutive days by stomach tube.

Monkey No.	Dates of Feeding	Allen-Doisy Units	Duration of Epithelial Growth, Days	Duration of Menses, Days	Time Between Feeding and Menses, Days
38	5/24/30 to 5/29/30	225	5	0	0
40	5/24/30 to 5/29/30	225	5	3	18
60	5/24/30 to 5/29/30	225	4	0	0
64	5/24/30 to 5/29/30	225	7	3	17
65	5/24/30 to 5/29/30	180	0	0	0
67	5/24/30 to 5/29/30	180	0	0	0
68	5/24/30 to 5/29/30	180	0	0	0
69	5/24/30 to 5/29/30	135	0	0	0
70	5/24/30 to 5/29/30	135	0	0	0
71	5/24/30 to 5/29/30	135	0	0	0
73	5/24/30 to 5/29/30	90	0	0	0
75	5/24/30 to 5/29/30	90	0	0	0
76	5/24/30 to 5/29/30	90	0	0	0

SUMMARY

A total of 64 monkeys were given Amniotin by stomach tube. In 33 of these when 400 or more units were given menstruation resulted. In 2 of 4 monkeys on 225 units bleeding occurred. The remaining 27 on lower dosages did not respond. There was no difference in the amount necessary whether the commercial preparation was used or a special glycerin alcohol solution.

A total of 23 monkeys were injected twice daily for 6 days. Eleven of these menstruated on dosages of 68 units or over. The remainder gave negative results.

Apparently then about 400 Allen-Doisy units are necessary when given by stomach tube to produce menstruation. About 75 units when injected will do the same thing. So the ratio between the oral and subcutaneous dosage is about 5 :1.

In all our work with amniotin in monkeys, whether given by injection or by vaginal pessaries or by the oral route, it is apparent that a certain threshold amount must be administered to obtain the menstrual reaction. Any excess of that amount does not produce any greater effect nor any undesirable symptoms.

Book Reviews

TESTICULAR GRAFTING FROM APE TO MAN. Serge Voronoff and George Alexandrescu. Translated by Theodore C. Merrill. Bretano's Ltd., London.

The scope of the book is sufficiently indicated by the title. Statistics are presented in 475 cases in which satisfactory postoperative reports were available. Results were considered successful if favorable effects persisted more than two years. In completely satisfactory operations the effects are stated to persist about six years. Among the various types of patients treated success is reported in from 22 to 91 per cent of the cases.

The book is well printed and the illustrations are clear.

LES SYNDROMES ENDOCRINES. R. Porak, 1929. G. Doin & Cie, Paris. Pp. 354. 2nd Edition.

The author has edited the second edition of this book in the same critical manner that characterized the first. He has evaluated the observations that have been made in Europe and in North and South America. His observations have been confirmed in the last four years as shown by publications in France and abroad. However, the endocrinologists are divided, the sceptics and the enthusiasts, the author belonging to the sceptical group. At the conclusion of his work the opinions of the enthusiasts are given and the reader has the two points of view presented for his consideration.

L'ENDOCRINOLOGIE ET LES ETATS ENDOCRINE-SYMPATHIQUES. II. A. C. Guillaume. 1929. G. Doin & Cie, Paris. Pp. 413.

With delightful clarity the author has set forth a great deal of material on the clinical aspects of endocrine disorders. The work represents, largely, however, an organization of much premature generalizing. Preciseness and clarity in this case are in their suggestion misleading because our knowledge of clinical endocrinology is neither precise nor clear. A false sense of security is also engendered by singling out for formal treatment under exact denomination a considerable number of the thousands of possible combinations of endocrine disorders. The formal bibliography includes some of the best and some of the worst monographs that have had wide currency. To the reader who can bring to bear an adequate critical judgment, the book can be commended as a source of much interesting information. It is marked as much, however, by omissions as by inclusions of important matter.

L'ENDOCRINOLOGIE ET LES ETATS ENDOCRINO-SYMPATHIQUES. III. LA CLINIQUE DES ENDOCRINES LES ETATS VISCERAUX. Guillaume, A. C., 1930. G. Doin & Cie., Paris. Pp. 597.

This third volume completes the work. It is devoted to the study of the endocrine-sympathetic system—sex, circulation, liver, nerve and mental disturbances. As in the two preceding volumes, this work differs from

similar works along this line in that the endocrines are not studied gland by gland but the disturbances are presented in the manner in which they appear in the clinic; that is to say, the thyroid, suprarenal, sex glands, etc., are not studied as such but as their disturbed functions appear in such diseases as rheumatism, menstrual disorders, cachexia, convulsions, circulatory trouble, etc.

ENDOCRINOLOGIA Y CRIMINALIDAD. M. Ruiz-Funes. 1929. Javier Morata, Madrid. Pp. 352.

Professor Ruiz-Funes of the University of Murcia has brought together and discussed philosophically a large mass of data from the world's literature on the endocrine factors that may be operative in criminality. The work includes chapters on the anthropology of the criminal; general endocrine data pertaining to the thesis; the relation of endocrinology to morphology, psychology, pathology, criminology in general, sexual manifestations and delinquencies; and the medico-psychological examination of criminals. The book closes with a unique bibliography of ten pages.

The work is one that must command the attention of all who are seriously engaged in a study of the biology of criminality. Such workers will find a large body of data brought to a focus on their problems.

Abstract Department

Note on the asthenia following decapsulization (Sur l'asthénic consécutive a la destruction des glandes surrénales). Abelous, J. E. and H. Lassale, Compt. rend. Soc. de biol. **101**: 998. 1929.

In decapsulated toads and frogs there is a disturbance of the response of nerve and muscle to electrical stimuli, heterochronism. This is due to the curare-like effects of the poisons which accumulate when the adrenals are lacking.—J. C. D.

Effects of long continued administration of adrenalin. Affleck, A. M., J. Pharmacol. & Exper. Therap. **36**: 301. 1929.

Rabbits tolerated daily injections of adrenalin up to 2 mgm. as long as 120 days, as indicated by failure to alter the curve of hyperglucemia.—C. I. R.

Influence of glycerine extracts from adrenals of rabbits with epithelioma on the evolution of this experimental epithelioma in white mice (Modifications évolutives de l'épithélioma expérimental de la Souris blanche par injection d'extraits glycérinés de surrénales provenant de Lapins préparés avec ce même épithélioma). Arloing, F., A. Josserand and J. Charachon, Compt. rend. Soc. de biol. **101**: 1140. 1929.

Such extracts when injected daily arrested the growth of the tumor. Extracts from uninoculated rabbits were ineffective.—J. C. D.

Pathologic anatomy in twenty-eight cases of Addison's disease. Barker, N. W., Arch. Path. **8**: 432. 1929.

During the past eighteen years at the Mayo Clinic necropsy has been performed in twenty-eight cases in which the clinical syndrome of Addison's disease has been present. The protocols of these cases were reviewed and all the material available was re-examined. In twenty-five of the twenty-eight cases there was a lesion of the suprarenal glands which on histological examination was called tuberculosis. In the sections of all these cases there were typical areas consisting of tubercles with endotheloid cells, giant cells, fibroblasts and lymphocytes. Acid-fast bacilli morphologically resembling bacilli of tuberculosis were found in these sections in eleven cases out of the fourteen cases in which the necropsy was done in 1925 or later. Acid-fast bacilli were not found in sections of the suprarenal glands from necropsies done prior to 1925. The tuberculosis of the suprarenal glands was found to be bilateral in all of the twenty-five cases and involved the entire gland with almost complete destruction. Some cortical tissue was found in all of the twenty-five cases except one in which there was incomplete material for study. This remaining cortical tissue was seen only as small islands or as cortical adenomas. The amount of suprarenal cortical tissue remaining was always very small compared to the normal amount and was estimated as less than 5% of this. The remaining three of the twenty-eight cases of Addison's disease which were studied had advanced atrophy of the suprarenal glands. Healed tuberculosis lesions of the lungs were found in all the cases in which there was tuberculosis of the suprarenal glands. Active tuberculosis of other organs was found in twenty-two of these. The weight of the heart was less than the average normal in fourteen of twenty cases in which data on the weight of the heart was available. Diffuse degenerative changes in the renal tubules were present in nine cases. In ten cases, including the three cases of suprarenal atrophy, the thymus was enlarged and there was hyperplasia of lymphoid tissue in the nodes and intestinal tract. There was scattered lymphoid hyperplasia in eight other cases. Seventy-three cases in which there were suprarenal lesions but in which clinical evidence of Addison's disease was lacking were briefly presented. These included the following: primary suprarenal neoplasms, fifteen cases; secondary suprarenal neoplasms, thirty-nine cases; atrophy, two cases; amyloidosis, three cases; infarction, two cases; hemorrhage, three cases; abscess, one case, and tuberculosis with incomplete destruction, eight cases.—Author's Abst.

Addison's disease. Bell, H. J., Penn. Med. J. **33**: 391. 1930.

The patient described was a white male aged 28. On May 1, 1929, he was seized with an attack of acute pain over the right costal margin extending into the right shoulder and lasting a few hours. Immediately afterward relatives and friends observed that he was developing what they described as "bad color." Several days later there occurred gastro-intestinal discomfort, anorexia, nausea, irregular attacks of vomiting, diarrhea and vertigo. The bad color continued to increase and deepen. On physical examination the patient, who in good health weighed between 160 and 170 lbs., was reduced to 147. The skin was dry and presented a distinct smoky hue in irregular patches covering his face, hands, back and about both axillae. The abdomen was retracted. The tongue was heavily coated; temperature was 96° F., the pulse rate 76. The systolic blood pressure was 78, the diastolic 56. A tentative diagnosis of Addison's disease was made. During the next two weeks the symptoms, particularly those referable to the gastro-intestinal tract, persisted without response to efforts directed toward their relief. The weakness became increased, the color of the skin deepened, and on July 13, following progressive intensification of subjective and objective symptomatology, death occurred from exhaustion. Antopsy was refused.—I. B.

Relation between the effects of adrenin on the arterial pressure and the place of injection (peripheral veins, portal vein and peripheral arteries) (Action de l'adrénaline sur la pression artérielle et lieu d'injection veins périphériques, veine-porte et arteres périphériques).

Changes in glycemia and the white blood cells following injection of adrenin into the circulation (La glycémie et le comportement des globules blancs du sang périphérique après injection d'adrénaline dans la circulation). Borysiewicz, A., Compt. rend. Soc. de biol. **102**: 97, 99. 1929.

Injection into a vein, peripheral or portal, of dogs is followed by a rise in blood pressure, while no such rise follows introduction in a peripheral artery. Increase in blood sugar and in number of white corpuscles follow the introduction of adrenin regardless of the site of injection, though the results are not identical. These results show that adrenin is not destroyed by the liver or the cells of the peripheral tissue, but is lost passing through the capillaries.—J. C. D.

Absorption of epinephrine from the subcutaneous tissue of the rat. Cori, C. F. and G. T. Cori, Proc. Soc. Exper. Biol. & Med. **27**: 558. 1930.

Intravenous injections of 0.001 mgm. of epinephrine per kilo per minute were always followed by a rise in blood pressure in amytal anesthetized rats. Subcutaneous injection of 0.2 mgm. per kilo made shortly afterwards had no effect on blood pressure but did produce hyperglycemia. The rate of absorption from the subcutaneous tissue of the rat must thus be less than 0.001 mgm. per kilo per minute, and greater than 0.0002 mgm. per kilo per minute, since this amount intravenously is the smallest amount which produces hyperglycemia in rats. By extraction of the subcutaneous tissue at the site of an injection and testing for epinephrine content by the Folin-Cannon-Dennis method it was found that epinephrine was still present 3 hours after the injection. Hyperglycemia also persists for at least 3 hours.—M. O. L.

The replacement of depleted adrenalin in the suprarenals. Crawden, G. P., J. Physiol. **68**: 313. 1929.

After depletion of adrenalin by cold, restoration in both normal and denervated glands proceeds at an equal rate. Nervous control is not necessary for recovery.—C. I. R.

A comparative study of the effect upon rat and rabbit tissue of ephedrine sulphate, epinephrin hychochloride and an adrenalin-like substance. Doty, E. J., J. Pharmacol. & Exper. Therap. **36**: 519. 1929.

The adrenalin-like substance was identical with epinephrine except for the absence of one hydroxyl group. No gross or microscopic pathology was discovered in any of the animals after prolonged administration.—C. I. R.

The hormone of the adrenal cortex. Hartman, F. A. and Katherine A. Brownell, Proc. Soc. Exper. Biol. & Med. **27**: 938. 1930.

Hartman reports further characteristics and properties of his extract of adrenal cortex by the use of which completely adrenalectomized cats may be kept alive in good condition indefinitely. In one cat receiving an inadequate supply of the extract the final stages of prostration, with dyspnea and convulsive twitchings had developed. Within 100 minutes after a dose of the extract the animal had recovered sufficiently to eat its usual quantity of food.—M. O. L.

Report of a case of paroxysmal hypertension cured by removal of an adrenal tumor. Porter, M. F. and M. F. Porter, Jr., Surg. Gynec. Obstet. **50**: 160. 1930.

This is apparently the second case reported in which diagnosis was made before operation. Malignant invasion of chromaphil-cell tissue seems to lead to hyperfunction.—A. T. C.

On the function of the adrenals. Rogoff, J. M., Endokrinologie, **5**: 256. 1929.

The author reviews the work of himself and colleagues which he interprets as contravening the idea that the adrenal medulla has any significant function. His work, however, is in accord with that of others as indicating an important function for the cortex. He suggests renaming the hormone of the adrenal cortex "interrenalin" and reports successful efforts to obtain an active extract containing this hormone.—R. G. H.

Adrenal extracts as regulators of iron metabolism (L'extrait de surrénales régulateur du métabolisme ferrique). Sokoloff, B., Compt. rend. Soc. de biol. **101**: 1098. 1929.

Iron combined by dialization with extract of the entire adrenal had a stimulating and regulating effect in dilute solutions on the regeneration of certain infusoria, but in concentrated solution produced liquefaction of the cytoplasm.—J. C. D.

The action of ephedrine, pseudoephedrine and epinephrine on the bronchioles. Swanson, E. E., J. Pharmocol. & Exper. Therap. **36**: 541. 1929.

Changes were recorded by an intrathoracic plethysmograph in pithed dogs. The three drugs produced broncho-dilatation which was not abolished by ergotoxin, ergotamine or atropine.—C. I. R.

An aqueous extract of the suprarenal cortex which maintains the life of bilaterally adrenalectomized cats. Swingle, W. W. and J. J. Pfiffner, Science, **71**: 321. 1930.

This preliminary report indicates that the authors have succeeded in obtaining a satisfactory extract. Its preparation is described.—R. G. H.

Further observations on adrenalectomized cats treated with an aqueous extract of the suprarenal cortex. Swingle, W. W. and J. J. Pfiffner, Science, N. S. **71**: 489. 1930.

The authors report further strikingly successful work with their cortical extract. Epinephrectomized cats have maintained perfect health up to 100 days of age, then upon discontinuance of the extract have soon developed acute, fatal adrenal deficiency. Other animals allowed to develop pronounced signs of deficiency immediately after adrenal excision have within four days been restored to health. The extract is stable in benzene or alcoholic solution.
—R. G. H.

Comparative effects of ephedrine and epinephrine on blood pressure, and respiration with reference to their alteration by cocaine. Tainter, M. L., J. Pharmacol. & Exper. Therap. **36**: 569. 1929.

Responses to ephedrine tend to decrease with successive doses, while the responses to epinephrine tend to increase.—C. I. R.

Glands of internal secretion and dementia praecox (Contribuiçao para o estudo das glandulas de secreçao interna na demencia prococe). Cesar, O., Memorias do Hospital de Juquery, S. Paulo, Brazil, **5-7**: 119. 1929.

The author studied at post mortem the endocrine glands of 11 subjects of dementia praecox of whom 7 had died of pulmonary tuberculosis, 2 of enteritis, 1 of pneumonia and 1 of dysentery. The ages ranged from 26 to 46 years. The material was fixed in formol or Bouin's fluid. Various routine stains were used. Results: In general the thyroid showed sclerosis, adenomas or colloid goiter; the testes, sclerosis, diminution of interstitial cells and absence of spermatogenesis; the adrenals showed no systematic alterations though the majority showed augmented lipoids.—R. G. H.

Endocrine factors in dermatoses. Various Authors.

An interesting series of abstracts on this general topic is published in Endokrinologie, **6**: 148. 1930.—R. G. H.

Sex differences in the cholesterol content of tissues. Chamberlain, E. N., J. Physiol. **68**: 259. 1929.

The cholesterol content of the suprarenals, ovaries, spleen, kidney, liver and brain were determined in rabbits of both sexes. Ten of the 19 females were pregnant from 6 to 28 days. The results were inconclusive for all the organs except the suprarenals and ovaries. Normal females showed an average of 66% more cholesterol in the suprarenals than the males. In pregnancy this excess largely disappeared. The ovaries were very rich in cholesterol but the percentages in pregnant and non-pregnant animals were about equal, but the absolute amounts must have been greater in the pregnant females since the ovaries averaged more than twice the weight of those of non-pregnant females. The author suggests that cholesterol is elaborated by the suprarenals of females in order to meet special requirements of pregnancy in building new tissue and that the ovaries supplement this function.—C. I. R.

Endocrinologic interpretation of normal weight, height and proportions. Engelbach, W., Endokrinologie, **5**: 28. 1929.

A valuable compilation of data on human growth, size, proportions and ossification at different ages. It can not be adequately abstracted.—R. G. H.

The relation of endocrine organs to polyglobulia, and a clinical type, probably of hormone origin (Uber die Beziehung endokriner Organe zur Entstehung der Polyglobulie und uber klinische Typen hormonal bedingter Polyglobalie). Gunther, H., Endokrinologie, **4**: 96. 1929.

Endocrine glands, according to their ability to increase the number of the red corpuscles, are arranged as follows: suprarenals, sex glands, hypophysis, thyroids, adrenal organ and spleen. Clinical conditions make it difficult to determine the part each plays since they are interacting. The second part of the paper is given over to a discussion of the hyper-suprarenalism, cases of which were observed. Most of these, including both male and female patients, showed an excess of red corpuscles. There is therefore probably a relationship between the suprarenal and polyglobulia.—B. C.

Physiology of the corpus luteum. VI. The production of progestational proliferation of the endometrium of the immature rabbit by progestin (an extract of the corpus luteum) after preliminary treatment with oestrin. Allen, W. M., Am. J. Physiol. **92**: 612. 1930.

Progestational proliferation can be induced regularly in the uterus of the immature rabbit weighing from 575 to 1647 grams by the injection of progestin if the uterus is first brought under the influence of oestrin. If, however, the animals are not treated with oestrin before the administration of progestin, only a very small percentage of them respond to progestin treatment.
—Author's Abst.

Studies on the influence of castration on the anal scent glands in rabbits (Etude de l'influence de la castration sur les glandes anales odorantes du Lapin). Badesco, M., Compt. rend. Soc. de biol. **102:** 527. 1929.

These glands are present but differ in appearance in the two sexes. Castration causes a change toward an indifferent type of gland, so that those of the castrated male and female resemble one another closely.—J. C. D.

The valuation of the ovarian hormone (folliculin) (Sobre la valoración de la hormona ovarica [foliculina]). Banti, L., Rev. sud-am. de endocrinol. **12:** 767. 1929. Abst., Chem. Absts. **24:** 1150.

The ovarian hormone is soon destroyed in the organism. Repeated very small doses are better for producing estrus in the spayed rat than few larger injections. As solutions in oil are slowly absorbed, generally fewer injections are sufficient, but this cannot be established as a rule. To adapt the test to conditions for the practical use of the preparation, the suggestion is made to give H_2O and oil solution in three injections at intervals of 24 hours.

The endocrine activity of the ovaries and disturbances of the menopause (L'activité endocrinienne des ovaires et les troubles de la menopause). Béclere, A., Presse méd. **37:** 1363. 1929.

The temporary or final cessation of the endocrine function of the ovaries causes the appearance of the disturbances of the menopause. Simple amenorrhea without any other trouble than the absence of the menstrual flow is compatible with and often exists with the persistence of the endocrine function of the ovaries. Amenorrhea with menopausal disturbances is a sure sign of the temporary or final cessation of this function.—J. Gagnon.

Note on the physiological properties of corpus luteum extract (Contribution a l'étude des propriétés physiologiques des extraits de corps jaune). Brouha, L. and H. Simonnet, Compt. rend. Soc. de biol. **101:** 366. 1929.

A water soluble lipoid free extract of corpora was used. In selected doses it suppressed the oestrous cycle in rats, while in smaller doses it produced changes similar to pseudogestation. It had no influence on the genital tract of spayed animals. If it was injected in spayed females after a dose of folliculine large enough to re-establish the oestrous cycle, it nullified the effect of the folliculine. If both extracts were injected simultaneously, the corpus luteum extract had no effect on the stimulating influence of the folliculine.—J. C. D.

On the clinical use of the ovary-stimulating hormone of the placenta. Preliminary report. Campbell, A. D. and J. B. Collip, Canad. M. A. J. **22:** 219. 1930.

Using the placental hormone preparation described in a previous paper in selected cases of ovarian hypofunction, definite results of an encouraging character have been obtained in five cases of oligo-menorrhoea, two cases manifesting distressing menopausal symptoms, and in two of dysmenorrhoea. A case exhibiting menopausal symptoms after pan-hysterectomy received no benefit.—A. T. C.

The development of the right gonad of the domestic fowl after ovariectomy; its physiological consequences (L'évolution de la gonade troite de la poule domestique après ovariectomie; ses conséquences physiologiques). Caridroit, F., Am. J. Physiol. **90:** 307. 1929.

The normal domestic fowl has only one ovary situated in the left side of the abdomen. The complete removal of the ovary makes a neutral animal with a cock's plumage but with the small comb, and spurs of the hen. Ovariectomy of the fowl often has as a consequence the development of the right gonad, which has remained in an embryonic state, into a testicle or less frequently an ovari-testicle. The bird in the latter case presents the appearance of a true gynandromorph with the hen's plumage and the cock's comb, if the necessary tissues are present in sufficient quantities.—J. Gagnon.

Sex hormones of the female. A review. Collip, J. B., Canad. M. A. J. **22:** 212. 1930.

The review deals with oestrin of the ovary, the control of ovulation by the internal secretion of the anterior lobe of the pituitary, and the possible occurrence of internal secretions in the placenta.—A. T. C.

The ovary-stimulating hormone of the placenta. Preliminary paper. Collip, J. B., Canad. M. A. J. **22**: 215. 1930.

At B. P. Wiesner's request, Collip undertook the further purification of the former's sulphosalicylic acid extract of placenta, and has succeeded in obtaining micro-crystalline fractions of great potency, although it is still uncertain whether they are a pure chemical compound. The preparation is active by oral administration in dosage which is not more than two or three times the effective subcutaneous dose. It does not appear to be destroyed by peptic or tryptic digestion in vitro. Immature white rats are stimulated by this preparation to oestrus, which then usually becomes cyclic. Injection into adult castrates is without effect, and injection into adult vigorous normal females has little effect on the normal oestrus cycle. Injections of moderate doses into pregnant rats do not affect the normal termination of pregnancy; this negative result may be due to size of dose and the point is being further investigated. The results suggest that in clinical use only those individuals showing definite evidence of hypoactivity of the ovary may expect to receive benefit from this placental hormone. It is considered probable that the hormone is elaborated in the placenta and is not the internal secretion of the anterior pituitary simply stored in the placenta.—A. T. C.

The psycho-physiology of a castrated dog (Sur la psycho-physiologie du chien privé de testicules). Combemale, P., Compt. rend. Soc. de biol. **101**: 1133. 1929.

This is a description of the differences, including lack of aggressiveness, jealousy, and boisterousness, as seen in dogs where both castrate and litter mate control were living in the house as pets.—J. C. D.

Isolation of the relaxative hormone on the corpus luteum. Fevold, H. L., F. L. Hisaw and R. K. Meyer, Proc. Soc. Exper. Biol. & Med. **27**: 604. 1930.

Purification of hormone of corpus luteum responsible for progestational development and other reactions. Id. 606.

Procedures are described for the extraction, separation and partial purification of 2 hormones of the corpus luteum; one causing relaxation of the pelvic ligaments and the other causing inhibition of ovulation, vacuolation of the vaginal mucosa in rats and the production of the premenstrual endometrium in monkeys.—M. O. L.

The position of the ovarian hormone in the hormone series (Uber die Stellung des Ovarialhormones in der Hormonreihe). Csepai, K., A. Fornet and S. Pellathy, Endokrinologie, **3**: 361. 1929.

Clinical studies of menformon which is presumed to contain the ovarian hormone indicate that the ovarian hormone is more nearly like insulin than adrenalin since it decreases the sympathetic tonus, blood sugar, and blood pressure.—B. C.

Female sex hormone. Frank, R. T. and M. A. Goldberger, J. A. M. A. **94**: 1197. 1930. Abst., A. M. A.

Frank and Goldberger assert that a lower renal threshold has been demonstrated for the excretion of the female sex hormone in amenorrhea and functional sterility, and evidence is adduced suggesting the existence of a general law governing the urinary threshold excretion of all hormones.

The male hormone. Funk, C., B. Harrow and A. Lejwa, Am. J. Physiol. **92**: 440. 1930.

The urine of young men contains a hormone (or hormones?) which induces comb growth in capons when a properly prepared extract of such urine is injected. The extracts obtained from testicles, when injected, also give definite but less marked effects. The difference may depend upon the amount of material used. Administration per os also has some effect, but the effect is much less pronounced and less constant than when the extract is injected. The male and female hormones show marked similarity in chemical properties. Both may be extracted with chloroform; both form alkaline salts; both are found in the fatty acid fraction; and the methods of purification so far adopted apply to both hormones.—Authors' Summary.

The results of testicular transplantation in Brown Leghorn hens. Greenwood, A. B. and J. S. S. Blyth, Proc. Roy. Soc. B. **106**: 189. 1930.

Both of the testes from a brother or chick of approximately the same age were implanted into a female of 6-39 days of age. The grafts were placed in a cavity between the anterior end of the kidney and the ribs. Of the 17 birds which received transplants, 10 showed no change except transient modifications. In 5 of the birds the combs resembled those of a juvenile male, spurs were developed, and plumage assumed the juvenile male type. The shape of the eggs laid by one of the groups (2 birds) was abnormal, the eggs being long and thin.—E. L.

Cowper's gland as a testis hormone indicator. Heller, R. E., Proc. Soc. Exper. Biol. & Med. **27**: 751. 1930.

The use of Cowper's gland in castrated rats is suggested as a qualitative indicator for testis hormone. Castration has a marked effect on Cowper's gland. In the rat after 20 days castration, a degeneration and merging together of most of the tubules and a lowering of the epithelium occurs, after 60 days there is a marked decrease in the gross size. Injection of testis extracts gave notable effects, including a return of the epithelium to the normal type. Relatively large amounts of hormone were necessary to keep the glands in normal condition.—M. O. L.

Production of a premenstrual endometrium in castrated monkeys by ovarian hormones. Hisaw, F. L., R. K. Meyer and H. L. Fevold, Proc. Soc. Exper. Biol. & Med. **27**: 400. 1930.

Five sexually mature female monkeys were castrated and then brought into full oestrum by the injection of follicular hormone. Such animals do not show the typical premenstrual development of the uterine endometrium. The additional injection of corpus luteum extracts, however, produced typical premenstrual changes in the endometrium.—M. O. L.

A forty-eight hour test for the female hormone with capon feathers as indicator. Juhn, Mary and R. G. Gustavson, Proc. Soc. Exper. Biol. & Med. **27**: 747. 1930.

The possibility is suggested of using as a test for the female hormone, the appearance of pink pigment at the base of the breast feathers of capons (the pigment is normally black in the species used) as a response to the hormone.—M. O. L.

Effect of serum from pregnant women on the estrual cycle of the guinea pig. Kelly, G. L. and L. Florence, Surg. Gynec. Obst. **50**: 435. 1930.

On the belief that during pregnancy there is an excess of corpus luteum hormone over the estrus-producing hormone in the circulating blood and on the basis of knowledge that estrus is inhibited by the corpus luteum hormone, experiments were undertaken to learn whether injections of serum from pregnant women would delay the onset of estrus in the guinea pig. Three groups of animals were used, the first as test animals and the other two as controls. The latter two received respectively serum from nonpregnant women and 1% peptone solution. The amount of serum injected in the first two groups varied from a total of 12 cc. to 20 cc., given over four days with increasing dosage daily. The third group received 20 cc. of peptone solution in four days. In the first group (test animals), there was a delay of from three to eight days in the onset of estrus, with an average of six days. In the second group the postponement was from 0 to two days, with .8 average. In the peptone group there was no delay. No effort has as yet been made to determine whether the effects vary if the serum is obtained from women in early, middle or late pregnancy.—G. L. Kelly.

Basal metabolism and other observations following oestrin injections. Kunde, M. M., F. D'Amour, A. J. Carlson and R. G. Gustavson, Proc. Soc. Exper. Biol. & Med. **27**: 745. 1930.

Oestrin was prepared from urine of pregnant women and injected subcutaneously into 2 normal and 2 spayed female dogs in doses of 100 or 200

rat units for period of 10 to 39 days. The basal metabolic rate determinations were all within normal limits of variation. Congestion and enlargement of the external genitalia and hemorrhagic discharge from the vagina were observed in all 4 dogs, as was also mating behavior and copulation.—M. O. L.

Results of castration on the secondary sex characters of the guinea pig (Effets de la castration sur les caractères sexuels secondaires du Cobaye). Guimarais, A., Compt. rend. Soc. de biol. **102**: 250. 1929.

The external genitalia, the body size, and psychie of a grown male guinea pig remained normal for a year and a half following castration. On autopsy no traces of testicular tissue could be found.—J. C. D.

Therapeutical experiments on females with spontaneous dysgenesia (Experimentell-therapeutische Studien an Weibchen mit spontaner Zyklusinsuffi-Zienz). Loewe, S. and H. E. Voss, Endokrinologie, **3**: 343. 1929.

A condition previously reported as hypohormonic occurs in laboratory animals, particularly white mice. It can be relieved by a diet of ground oats, rye bread and "promonta," a commercial product containing vitamines, lipoids, etc. The presence of the disease is evidenced by cessation of oestrus; its relief by recurrence of oestrus.—B. C.

Effect of lutein feeding on the oestrus of the guinea pig. Macht, D. I. and A. E. Stickels, Proc. Soc. Exper. Biol. & Med. **27**: 427. 1930.

A series of guinea pigs were fed daily from 0.1 to 0.2 grams of desiccated corpus luteum substance from sows. There occurred definite inhibition of the oestrous cycles, with shortening of the oestrus and lengthening of the dioestrus periods.—M. O. L.

Experimentally induced intermenstrual bleeding in ovariectomized monkeys. Maddux, W. P., Proc. Soc. Exper. Biol. & Med. **27**: 873. 1930.

In 2 adult ovariectomized macaques bleeding was observed in the vaginal smear on the tenth to twelfth days of treatment with ovarian hormone given intravaginally in gelatine pessaries.—M. O. L.

Preconception ovarian radiation: Its influence on the descendants of the albino rat. Murphy, D. P., Surg. Gynec. Obst. **50**: 588. 1930.

A group of 51 albino rats was exposed to heavy ovarian radium treatments, before they were mated. Each of these animals later cast one or more litters. The total first generation young amounted to 402. Of these, 17 females gave birth to 91 offspring (second generation), after mating with brothers, or with males born of other irradiated mothers. No instance of abortion was observed in either generation. In the irradiated animals either sterilization resulted or else the treatment did not materially alter the frequency with which subsequent conceptions followed one another. Litter size was diminished by maternal ovarian irradiation, the earliest litters being the smallest. The first generation young exhibited a delay in growth and fertility but presented no gross abnormalities which could reasonably be ascribed to the effect of the maternal irradiation. Likewise the second generation of offspring showed no evidence of ill health or underdevelopment which might be attributed to the grandmaternal irradiation.—Author's Summary.

The prolongation of pregnancy by extracts of corpus luteum. Nelson, W. O., J. J. Pfiffner and H. O. Haterius, Am. J. Physiol. **91**: 690. 1930.

Extracts of corpora lutea of pregnancy (sow) were successful, when administered subcutaneously, in prolonging the period of pregnancy in rats (13) for periods ranging from 30 to 150 hours. The young born 40 hours or more overtime gave evidence of a size larger than is characteristic of a pregnancy of normal duration. If the period of prolongation did not exceed 70 hours, the young were viable when born. In excess of this time still births occurred.—Authors' Summary.

Ovarian transplantation (with a report of thirty-one cases). Norris, C. C. and C. A. Behney, Surg. Gynec. Obstet. **49**: 642. 1929.

Ovarian transplantation is not a substitute for conservation of the ovary in its normal situation and should be reserved for those cases in which this is inadvisable. The life of a transplanted ovary is probably not more than 2 or 3 years. Grafts frequently become tender for a day or two each month, but rarely give serious trouble. The operation is practically without mortality or morbidity, and most of the grafts "take." When the menopause occurs it is generally more prolonged, gradual, and analogous to the normal menopause than if grafting had not been performed.—A. T. C.

Recent advances in physiology of menstruation. Novak, E., J. A. M. A. **94**: 833. 1930.

The author is of the opinion that radical readjustments must be made in our views as to the physiology of menstruation because of important new developments in this field. There is little doubt that in lower animals the sex cycle can occur independently of ovulation. The best evidence along this line has come from observations on monkeys, which menstruate much as do human females. Menstruation without preceding ovulation is certainly not the rule in women, but there is reason to believe that it occurs at times, though the associated endometrial cycle would naturally be different in such cases. Even if preceding ovulation is the rule, it is not certain that the two are related in the nature of cause and effect. The time has come when the doctrine of the "primacy of the ovum" in the regulation of menstrual periodicity must be abandoned. There is no reason to believe that any other constituent of the ovarian structure is any more important in this respect, but there is evidence to suggest, though not to demonstrate, that the pituitary may, by the probable periodicity of its own function, be the regulator of the menstrual rhythm. This, however, carries the problem only one step toward its solution, for it raises the question of what determines the periodicity of the pituitary, and still leaves the question of menstrual periodicity one of the mysteries of life. The dual nature of the ovarian secretion has been definitely established by the demonstration of an active corpus luteum extract, with properties in some respects antagonistic, in others supplementary, to those of the already well recognized ovarian follicle hormone. For various reasons, especially the fact that the characteristic secretion of the corpus luteum has very different properties from those of the follicle and the placenta, the term "gestational gland," to include these three structures, is incorrect, and should be abandoned. The most important recent contribution to sex physiology, and the one which promises most in its future practical applications, is the discovery that the anterior pituitary constitutes the "motor" of the ovary. The surprising effects of implantations of the anterior lobe on the growth and maturation of the follicular apparatus open up a vast field of possibilities. Although the discovery of the follicle hormone has as yet yielded almost nothing from a therapeutic standpoint, there is reason to feel that the discovery of the underlying role of the anterior pituitary secretion may, in the future, be more productive of results in the treatment of disorders of the sex cycle.—A. M. A.

Concerning the so-called hilus cells of the ovary (Uber die sogenannten Hiluszellen des Ovariums). Pawlowski, E., Endokrinologie, **3**: 321. 1929.

There are certain cells in the hilus of the functioning ovary which are easily distinguished by their morphology and lipoid content. They are not analogous to the interstitial cells of the testes. Because of their relation to the sympathetic nerves they are supposed to act through them. The name "hilus cells of Berger" is proposed for them.—B. C.

Experimental research on the ovarian hormone (Experimentelle Untersuchungen uber die Hormone des Eierstocks). Probstner, A. v., Endokrinologie, **3**: 338. 1929.

Oestrus, as determined by vaginal smears in ovariotimized rats, can be initiated by injection of fluid from ripe follicles, glandufolin and folliculine, but not by extracts of ovarian tissue without follicles, or by a number of commercial ovarian preparations. Transplants of human corpora lutea in various stages give positive results, while those of the cow do not. Oestrus is depend-

ent upon a hormone produced by the follicle; this hormone production is hindered by the production of a corpus luteum. In the absence of the hormone menstruation occurs. The periodicity therefore of oestrus depends upon the production of ripe ova. If ripe ova are not present the initiation of oestrus depends upon the introduction of the proper hormone, but if mature ova are present the initiation of oestrus depends upon the ripening time. The addition of the hormone then may only intensify oestrus but can not change its periodicity or rhythm.—B. C.

Cause of the increased blood pressure at the climacteric (Uber die klimakterische Hypertonie). Rutich, E. v., Endokrinologie, **3**: 255. 1929.

In order to determine whether or not the increased blood pressure at the climacteric is due to the decrease in ovarian hormone, the author adopted two methods, the clinical-statistical method and the gland therapy method. The glandular substance, menformone, glandufolin, et al., were given by injection. He concludes as a result of both investigations that the cessation of ovarian function is not a primary cause of the increased pressure but that it may be an adjunct in cases where the vegetative nervous system is constitutionally disposed to lability. Glandular therapy has no effect.—B. C.

Treatment of ovarian insufficiency with sex hormone (Die Behandlung der Ovarialinsuffizienz mit Sexualhormon). Siebke, H., München med. Wchnschr. **76**: 1752. 1929.

Two forms of ovarian insufficiency are recognized by the author. The vegetative, representing a failure of maturation of the genitalia and of secondary sexual characteristics, and the generative, irregularity in menstruation due to a derangement of ovulation. On the basis of this classification two tests have been devised in determining the efficacy of any hormonal preparation in the human female. These are the "growth test" by which growth of hypoplastic organs to maturity must be achieved, and the "menstrual cycle test," the institution of a normal menstrual rhythm. Menformon, the preparation selected for this series, was used in 20 cases according to the scheme of dosage worked out by Laqueur. They comprised cases of amenorrhea, metrorrhagia, and dysmenorrhea with or without genital hypoplasia and increasing obesity. As the result of treatment, 12 of these satisfied one or both tests with alleviation of symptoms. They included 4 amenorrheas. Of the failures 5 were obese individuals showing stigmata of pluriglandular disturbances and in these anterior lobe pituitary hormone (prolan) also was ineffectual. In 1 case the growth test was positive but the symptom of which the patient complained, dysmenorrhea, was not helped. The other 2 failures were insufficiently treated and could not be properly controlled. The selection of the proper cases for treatment is stressed. Inflammations, tumors, position changes, and general constitutional conditions must be ruled out. Since cases of pluriglandular disturbances as well are not benefited, the number of cases in which sex hormone therapy is indicated must remain relatively small.—F. Spielman.

On the reactivation of the senile testis of the rat by means of injections of gonadotrope hormones. Wiesner, B. P., Edinburgh M. J. **37**: 229. 1930.

Four animals were used and the result with one of them is given in detail. Injections of the author's protein-free extract of human placenta, or of extracts of cattle anterior lobe, resulted in the apparent return to activity of the prostate and the seminal vesicles, the enlargement of the testis, and the increase therein of the formation of mature spermatozoa. This was checked by removing one testis at the start of the experiment and comparing it with the remaining gland at the end. The author emphasizes the part played by gonadotropic hormones acting on the testis from outside, in cases of rejuvenation.—J. C. D.

Egg-laying in Triturus viridescens following pituitary transplants. Adams, A. Elizabeth, Proc. Soc. Exper. Biol. & Med. **27**: 433. 1930.

Female urodeles, Triturus viridescens, were caused to deposit eggs out of season by intramuscular or intraperitoneal transplants of whole pituitary or anterior lobe. Posterior pituitary or muscle transplants were without effect.
—M. O. L.

A comparative study of the anterior hypophysis in the pregnant and non-pregnant state. Bacon, A. R., Am. J. Obst. & Gynec. **19**: 352. 1930.

The hormone content of the anterior hypophysis of pregnant and non-pregnant cattle was compared by transplanting weighed pieces of the glands ranging from 5 to 50 mgm. into infantile female white mice, and comparing the quantity of gland required to produce premature estrus, as determined by vaginal smears (Allen and Doisy's procedure). Contrary to expectations, it was found that the anterior hypophysis of non-pregnant cattle was the more active. The anterior hypophysis of foetal calves had a very low hormone content, only two larger transplants out of 21 being positive. It is concluded that the great increase in anterior pituitary hormone in the circulation during pregnancy in all probability arises elsewhere than in the hypophysis.—Author's Abstract.

Early changes produced in dogs by the injections of a sterile active extract from the anterior lobe of the hypophysis. Benedict, E. B., T. J. Putnam and H. M. Teel, Am. J. M. Sc. **179**: 489. 1930.

Four dogs were injected with a sterile alkaline extract of the anterior lobe of the hypophysis. Twenty figures of photographs of the animals, their genital tracts and organs are included in the paper. The genital tracts in both male and female were sexually inactive. Skeletal over-growth was produced by daily injections of three months duration. The animals after injection for two months showed sluggishness and a plantigrade stance.—E. L.

The functional significance of the parts of the hypophysis (Die funtionelle Bedeutung der einzelnen Hypophysenanteile). Biedl, A., Endokrinologie, **3**: 241. 1929.

A short survey of the structure and origin of the pituitary with a resume and evaluation of what is known at present about the functioning of the various parts of the gland.—B. C.

On the origin of acroparesthesia (Uber den Ursprung der Akroparästhesien). Borak, J., Endokrinologie, **5**: 8. 1929.

Acroparesthesia is a common symptom in acromegaly, in normal menstruation and at the menopause. This condition is amenable to x-ray treatment of the hypophysis. The condition is probably to be ascribed to vasomotor disturbances of hypophyseal origin.—R. G. H.

Effects of hypophyseal and follicular extracts on a young monkey (Action des extraits hypophysaire et folliculaire chez la Guenon impubère). Courrier, R., R. Kehl and R. Raynaud, Compt. rend. Soc. de biol. **101**: 1093. 1929.

Signs of precocious oestrous cycles were produced by injection of extract from beef hypophysis and by folliculine in a two-year-old macacus sylvanus. —J. C. D.

Chondrodystrophia (Uber Chondrodystrophie). Curschman, H., Endokrinologie, **4**: 161. 1929.

The author cites three cases of dwarfs, two of which are normal in general except for size. He is unable to account for them on hormonal basis. The sella turcica in each appears normal. He suggests that inheritance may be a factor, but is really at a loss to explain the cause of dwarfism. The third has excessive fat which is considered as a "coincidence."—B. C.

Contribution to the anterior hypophyseal reaction with special consideration of the Aschheim-Zondek pregnancy reaction (Beitrag zur Hypophysen-Vorderlappen-reaction unter Besonderer Berück Sichtigung der Aschheim-Zondekschen Schwangerschaftsreaktion). Ehrhardt, K., Klin. Wchnschr. **8**: 2044. 1929.

In a series of 400 clinically proven cases the Zondek-Aschheim pregnancy reaction was correct within an error of 1.5-2%. Need is expressed for a more

rapid test and the following attempts were made to speed up the reaction: (1) Spleenectomy; (2) Removal of one ovary; (3) Removal of one and both uteri; (4) Keeping rats at warmer temperatures. Except for an inhibition of Zondek-Aschheim reaction II and III in (3), the results were essentially negative. Hypophyseal implants were combined with implants of adrenal medulla, cortex of adrenal, whole adrenal, pancreas, pineal body, and thyroid. No definite synergistic or antagonistic action was demonstrated. Prähormon was injected with adrenalin, hypophysin, insulin, and thyroxin. The results are similar to those of the implant experiments. Implanted ovaries did antagonize hypophyseal implants and ovarian extract antagonized prähormon. Anterior hypophyseal hormone is found in the exudate of cantharidin blisters during pregnancy. It was also present in the cerebro-spinal fluid of three patients with eclampsia though not found in the C. S. F. of normal pregnant women. Many other tissues and plants were tested for anterior hypophyseal hormone action with negative results.—D. W. Gaiser.

Studies of the relation of the pituitary to watermetabolism. Goldzieher, M. A. and J. Kaldor, Proc. Soc. Exper. Biol. & Med. **27**: 799. 1930.

Guinea pigs were given novasurol as a diuretic. They lost 5.2% of their weight in 6 hours as compared with a normal loss of about 3.5%. The pigs were killed from 20 minutes to 6 hours after the novasurol injections and the hypophyses examined histologically. No changes in the structure of the posterior lobe were observed, but in the anterior lobe there was found a decrease in the number of eosinophile cells and of the amount of eosinophile substance, and a marked increase in basophile cells. The same results were obtained with the use of theobromin as a diuretic. The authors interpret these histological changes as indicating stimulation and increased activity of the anterior lobe cells.—M. O. L.

Growth and bone changes in rats injected with alkaline anterior pituitary extracts. Handelsman, M. B. and E. F. Gordon, Proc. Soc. Exper. Biol. & Med. **27**: 412. 1930.

Rats weighing over 175 grams injected with alkaline anterior pituitary extracts showed good growth response and a greater activity in periosteal bone formation than did their controls. The bone growth reaction consisted of an intensification of the activity of the normal periosteal ossification zones. Those animals that gained most in weight showed the greatest ossification response.
—M. O. L.

Hormones of the anterior pituitary lobe. Hewitt, L. F., Biochem. J. **23**: 718. 1929.

Dilute alkaline extracts were made from beef anterior pituitaries by a method similar to that previously described by Evans and Long in 1923, Teel in 1926, Putnam, Teel and Benedict in 1928, and Bellerby in 1928. Female white rats weighing 128 to 146 gm. were given intraperitoneal injections of 1 cc. each daily. On the average, injected rats grew at the rate of over 12 gm. per week while control animals never grew at a rate exceeding 6 gm. per week. Extracts which were made slightly acid before filtration were variable in growth stimulating properties, one extract producing growth while the next had no such effect. All the extracts, however, stimulated the development of corpora lutea and produced the so-called "mulberry ovary." Beef anterior pituitaries were extracted with N/10 acetic acid, neutralized and filtered. Such extracts had considerable growth stimulating effect upon mature rats but no stimulation of sexual development in immature mice. If the acid extract was shaken well with kaolin and then centrifuged, the supernatant liquid was capable of causing enlargement of uteri and ovaries and cornification of the vaginal mucosa in immature rats. An acid extract made with N/10 hydrochloric acid and shaken up well with kaolin before neutralization and centrifugation was tested on 2 rats. A mature rat showed no stimulation of growth in 2 weeks while an immature rat showed stimulation of sexual development.—E. P. Bugbee.

Effect of pituitary extracts on basal metabolic rate. Himwich, H. E. and F. W. Haynes, Proc. Soc. Exper. Biol. & Med. **27**: 815. 1930.

In starved male rats the basal metabolic rate was increased an average of 32% in the first hour after the injection of pitocin and 13% in the second and third hours. Pitressin in doses of 50 to 100 units per kilo decreased the oxygen consumption an average of 22% in the first hour. Variable effects were found with smaller doses. Surgical pituitrin also produced a decrease in oxygen consumption.—M. O. L.

Diabetes insipidus. Jackson, H. B., Proc. Roy. Soc. Med. **23**: 74. 1930. (Clin. Sect.)

The patient was a man 34 years old, admitted to the hospital January 31, 1930. His chief complaints were great thirst and frequency of micturition, of 6 months' duration. The frequency occurred diurnally and nocturnally, necessitating his getting up 3 or 4 times during the night. He complained also of becoming "nervy" and excitable. Apart from these symptoms he felt well. He did not suffer from lassitude, weakness, headache, vomiting or visual disturbances. Radiographic examination of the pituitary was negative. The patient responded satisfactorily to subcutaneous injections of pituitrin and one of its components, "vaso-pressin."—I. B.

Histology of the anterior pituitary of the foetal pig with reference to growth and maturity. Nelson, W. O., Proc. Soc. Exper. Biol. & Med. **27**: 596. 1930.

Basophile elements greatly predominated in the anterior pituitaries of foetal pigs at about the 10 cm. stage. At about the 20 cm. stage the basophile cells were less numerous than the eosinophils.—M. O. L.

Active principles of pituitary extracts and insulin effect on dogs (Influencia de las diversas substancias de la hipófisis sobre la acción insulínica en los perros normales). Magenta, M. A., Rev. Soc. argent. de biol. **5**: 89. 1929.

Oxytocin is the active principle in pituitary insulin antagonism. Vasopressin and an anterior lobe extract (Putnam, Teel, and Benedict's technique) does not modify the effect of insulin. Oxytocin causes a rise in blood sugar and the disappearance of symptoms in hypophysectomized dogs with severe hypoglycaemia through insulin injections.

Hormone of anterior lobe of hypophysis: Presence in placenta. Philipp, E., Zentralbl. f. Gynäk. **54**: 450. 1930. Abst., J. A. M. A. **94**: 1545.

Philipp implanted pieces of amnion, chorion and Wharton's jelly and injected amniotic fluid from pregnant white mice into sexually immature female white mice. In all of the animals the implantation or injection was followed by a hypertrophy of the uterine tubes and the ovaries and the appearance in the latter of a graafian follicle and numerous corpora lutea. The earlier the pregnancy, the more marked were the changes produced. Placental tissue from a mouse in the second month of pregnancy produced much more marked changes than placental tissue from a mouse in the fourth month of pregnancy. In one case, however, an intense reaction was produced by placental tissue from a mouse in the fifth or sixth month of pregnancy. Control experiments with implantations of pieces of fetal organs and umbilical cord tissue all gave negative results. On the basis of his experiments the author concludes that the placenta early in pregnancy contains a large amount of "anterior lobe hormone."

Treatment of pituitary tumors; rôle of roentgen ray and of surgery. Towne, E. B., Ann. Surg. **91**: 29. 1930. Abst. Arch. Physical Therapy, **11**: 141.

Five cases are reported by Towne which illustrate long-standing favorable results from roentgen treatment, and show that if the result is not good, a cystic tumor, favorable for surgery, may be diagnosed. He believes that the present custom of following surgery immediately with roentgen treatment confuses the issue. The two methods may be used separately without jeopardizing the patient's chance for a cure. He proposes that all pituitary adeno-

mas be treated by roentgen rays under the observation of the ophthalmologist and the neurosurgeon; that the treatment be stopped as soon as improvement begins, and that surgery be undertaken short of six months only when visual acuity and fields recede under roentgen treatment.

The action of anterior pituitary upon the x-rayed ovaries (Hypophysenvoiderlappenwirkung auf das strahlengeschadigtee Ovarium). Walter, A., Endokrinologie, **7**: 1. 1929.

Sixty infantile mice received dosages of 400-500 R and were thereby sterilized. Transplants of anterior pituitary were made from 3-4 weeks after radiation, with oestrus cycles resulting within 80-100 hours. Animals kept for longer periods of time (10-11 grams weight) showed regular oestrus cycles. Transplants in animals 3-4 months old in dioestrus gave excellent results. From these experiments the conclusion is reached that since irradiated ovaries can maintain an oestrus cycle followed by heat, the theca cells must either function as hormone carriers or hormone producers. Since egg cells or fresh corpora lutea can not produce oestrus, the interstitial cells gain in importance. The transplantation is effective only so long as eggs can be produced.—B. C.

Hormones of anterior lobe of hypophysis (Ueber die Hormone des Hypophysenvorderlappens). Zondek, B., Klin. Wchnschr. **9**: 245. 1930. Abst., J. A. M. A. **94**: 1272.

Zondek states that following repeated injections of fluid expressed from the anterior lobe of the hypophysis into rats, Evans observed an enormous growth of these animals. The sex hormone of the anterior lobe of the hypophysis does not have this influence. Consequently the author concludes that besides the sex hormone the anterior lobe of the hypophysis also secretes a hormone that influences the processes of growth. Other investigators observed that the specific dynamic action of food is regulated by the anterior lobe of the hypophysis. It was found that a certain extract of the anterior lobe effected a decrease in the metabolic rate and an increase in the specific dynamic action. The author further discusses the functions of the sex hormone of the hypophysis. Experiments revealed that the sex hormone consists of two different substances. The first one influences the ripening of the follicle. The other substance effects the formation of the corpus luteum. The author gives a diagrammatic sketch showing the action of the four hormones of the anterior lobe of the hypophysis, namely: (1) the hormone affecting growth; (2) the hormone that influences the ripening of the follicle; (3) the hormone that causes development of the corpus luteum, and (4) the hormone influencing metabolism.

Investigations on functioning of anterior lobe of hypophysis (Untersuchungen zur Funktion des Hypophysenvorderlappens). Zondek, B., Deutsche med. Wchnschr. **56**: 300. 1930. Abst., J. A. M. A. **94**: 1451.

Zondek first reviews the results of former researches on the hormones of the anterior lobe of the hypophysis, which were conducted partly by him and partly by other investigators. It has been found that, besides the sex hormone, the anterior lobe of the hypophysis also produces a growth hormone and a substance that influences metabolism. Careful investigations on the action of the sex hormone revealed that it is not an elementary substance but that it contains two factors, the first one effecting ripening of the follicles and the second one effecting luteinization. These two factors are designated as A and B, respectively. Investigation on the pregnancy reaction revealed that the factor A is not characteristic for pregnancy because it may also occur in the urine when pregnancy does not exist. The author succeeded in isolating the A factor of the sex hormone. He asserts that during pregnancy both factors are excreted in the urine in great quantities. However, the A factor occurs alone in the urine when the sex glands do not function properly, namely, after bilateral ovariectomy, and in the menopause. Therefore, the demonstration of this factor in the urine indicates that the sexual function has ceased. Factor A was also found in women with tumors of the genitalia. However, the presence of this factor is not an absolute indication of cancer because it is found also in cases of nonmalignant tumors.

Surgical treatment of hyperinsulinism. Allan, F. N. and W. C. Boeck, J. A. M. A. **94**: 1116. 1930.

Hyperinsulinism is a condition which may cause serious disability, and sometimes death. When the hypoglycemic tendency is so strong that the patient is incapacitated, surgical treatment is justified. Resection of the pancreas appears to be a logical method of treatment. In one case in which hyperinsulinism was due to tumor of the islands, operation was followed by relief from hypoglycemic symptoms. In four cases in which organic change in the pancreas was not demonstrable, the results of partial pancreatectomy were not entirely satisfactory; yet the improvement observed in three cases was encouraging. Hope of control of the disorder by surgical measures, in such cases, may lie in more radical resection.—Authors' Summary.

Diabetic coma: A report of eighty-one instances. Bowen, B. D. and I. Hekimian, Ann. Int. Med. **3**: 1104. 1930.

The blood sugar in 64 of these instances varied from 1320 to 266 mgm. It exceeded 400 mgm. in 53 instances. The leucocyte count exceeded 15,000 in 74 of the cases. The treatment consisted of 50 units of insulin subcutaneously and 1000 cc. of salt solution by hypodermoclysis. Sodium bicarbonate, 30-40 grams, was given by mouth or through a stomach tube. Insulin, after the initial dose, was given in doses of 10-30 units every 2-4 hours until the Benedict test solution began to retain some of its blue color. Nearly all the cases of coma showed some degree of circulatory insufficiency, which was treated with caffeine sodium benzoate or a digitalis preparation. Ten of these coma cases died from complications. Abdominal pain was an early symptom of coma. The authors believe that sodium bicarbonate is beneficial in the treatment of coma.—E. L.

Clinical significance of initial insulin hyperglycemia (Die Glinische Bedentung der initialen Insulinhyperglykämi). Bürger, M., Klin. Wchnschr. **9**: 104. 1930. Abst., J. A. M. A. **94**: 1026.

Bürger points out that it has been demonstrated that the blood sugar increases during the first twenty minutes following intravenous injection of insulin. This initial insulin hyperglycemia is especially marked if the insulin is injected directly into the portal vein or into one of its branches. However, if the liver circulation has been interrupted and insulin is injected into a peripheral vein, the initial insulin hyperglycemia does not develop. The author describes experiments on several groups of persons. Tests on healthy persons without disturbances of the liver revealed that after the insulin injection the sugar content of the blood was on the average 22% higher than before the injection. In patients with cirrhosis the initial insulin hyperglycemia reached only 2.7%, and in some instances it was entirely absent. Patients with severe cholemia showed an increase of only 5.7%, whereas in persons who had recovered from jaundice and in whom the bilirubin content of the blood was normal, the primary insulin hyperglycemia reached 14.5%. These tests prove that the development of initial hyperglycemia depends on the condition of the parenchyma of the liver. However, experiments on animals proved that it was also necessary that the glycogen depots of the liver should be full. Starving animals developed only a minor initial hyperglycemia. In patients with hyperthyroidism the primary insulin hyperglycemia was considerably less than in persons with a normal basal metabolism, whereas in patients with myxedema the initial hyperglycemia was in excess of that in healthy persons. In one individual with myxedema it was 70% higher than the sugar content before the insulin injection. The author reasons that in patients with hyperthyroidism the glycogen depots are exhausted as a result of an increased metabolism. On the other hand, in patients with hypofunctioning of the thyroid, there is an oversupply of glycogen because the metabolic rate is reduced. The author also examined patients with diabetes. He found that in those who previously had received insulin treatments and who adhered to a restricted diet the primary hyperglycemia was about like that in normal persons. In patients with diabetic coma, however, it was absent. It is assumed that this is due to the deficient glycogen content in the liver of comatose persons. In conclusion the author stresses that all these experiments were made with the same brand of insulin. Tests with other brands are now being conducted and it appears that the pharmacolo-dynamic properties are not the same in all brands.

The effect of shivering on respiratory quotient in pancreatic diabetes. Chaikoff, I. L. and J. J. R. MacLeod, Quart, J. Exper. Physiol. **19**: 291. 1929.

Dogs were completely depancreatized and maintained in good nutrition by feeding raw meat, raw pancreas and cane sugar, with insulin injections twice daily. After operation recovery, food and insulin were discontinued for a few days and resting metabolism determined. Then while the animal was shivering from a cold bath it was placed in a cabinet cooled to 10° to 13° C., and metabolism again determined. Normal fasting controls were similarly treated. In both groups oxygen consumption and the respiratory quotient were increased to about an equal degree. The high quotient was proven not to be due to discharging CO_2 combining power of blood before and during shivering. That protein metabolism was not increased was determined by urinalysis. It was concluded, therefore, that the high quotient was due to oxidation of carbohydrate which was not accompanied by gluco-neogenesis from fat. The failure of the quotient to remain high during the entire shivering period supports this conclusion. That the falling of the quotient was not due to decreased metabolism was indicated by the sustained increase in oxygen consumption. Carbohydrate can be utilized by both normal and diabetic dogs.—C. I. R.

The use of constant glucose injections for the study of induced variations in carbohydrate metabolism. II. The effects of insulin, pancreatectomy and nervous manipulations of the pancreas. Colwell, A. R., Am. J. Physiol. **91**: 679. 1930.

The administration of insulin diminishes, and of epinephrine increases, the excretion of sugar resulting from the constant injection of glucose by vein. With proper dosage these responses may occur with no corresponding changes in the blood-sugar concentration. Complete removal of the pancreas causes virtually all of a constant supply of glucose to be excreted in the urine. The effect appears gradually over a period of four to eight hours. Under amytal anesthesia the ability to utilize glucose is not impaired by stimulation of the major splanchnic nerve after removal of the corresponding adrenal gland and section of the hepatic nerves, by denervation of the pancreas, or by bilateral vagus section.—Author's Summary.

The use of constant glucose injections for the study of induced variations in carbohydrate metabolism. III. The fate of the retained sugar under normal conditions and after epinephrin and insulin. Colwell, A. R. and E. M. Bright, Am. J. Physiol. **92**: 543. 1930.

Working on cats under amytal anesthesia it was found that when glucose is administered intravenously at constant rates high enough to cause abnormal glycosuria, after the first three or four hours a constant proportion of it (usually about three-quarters under the present conditions) can be accounted for by oxidation and excretion, and occasionally also by conversion to fat. Two implications may be made from this fact: (a) glycogen storage eventually proceeds at a constant measurable rate; (b) after the initial period of adjustment of free sugar concentration in the tissues, all administered glucose not utilized is excreted promptly in the urine. Evidence is presented which indicates that insulin results in a transient increase in sugar combustion and a more prolonged augmentation of the rate of glycogen storage, and that epinephrin causes a net loss of glycogen from the body. Glucose oxidation is abolished by prolonged administration of epinephrin intravenously at a rate of 0.001 mgm. per kgm. per minute. This occurs in spite of a constant intravenous supply of glucose. Since glucose oxidation invariably occurs under identical conditions without epinephrin, the use of anesthesia in the present investigations is in no way responsible for the phenomena. Attempts to reproduce the results of pancreas removal in this manner have been inconclusive. It is not clear, therefore, whether the observed effect of epinephrin is due to a suppression of insulin production or not. Contemporary evidence favors the view that ordinary diabetes mellitus is a result of a functional disorder of the pancreas which is dependent upon a disease of the sympathetic nervous system, and that continuous excessive secretion of epinephrin may be an important intermediate factor in this mechanism.—R. G. H.

A clinical method of insulin assay (Eine klinische method zur Wertbestimmung von Insulin praparaten). Csepai, K. and B. Forstner, Endokrinologie, **3**: 412. 1929.

A normal person's reaction to insulin varies but little in the course of a few days, and it is proposed to use such an individual for insulin assay in preference to lower animals. Tests with standard solutions are run for three days, then the solution to be standardized is used, and the blood pressure effects compared. This is a desirable method especially where animals are not available.—B. C.

Complications of diabetes. Evans, F. A., Penn. M. J. **33**: 368. 1930.

The unavoidable complications of diabetes are always serious. Acute general infections carry a double menace—their own and the increased severity of the diabetic state which they invariably induce. With the fever and increased metabolism, perhaps with the over-stimulation of endocrine secretions antagonistic to the islands of Langerhans, sugar tolerance is so depressed that the diabetes can no longer be properly treated by dietary measures alone. Here insulin is practically always necessary. Gastro-intestinal disorders complicating diabetes present to the clinician problems that are usually not serious. Among these are constipation, diarrhea, achylia gastrica and gastric and duodenal ulcers. In these conditions surgical treatment should be instituted promptly and the relief of these complications may assist in the treatment of the diabetes. Thyroid disorders complicating diabetes create discouraging situations since the two conditions, diabetes and thyrotoxemia, require opposing dietetic management. Senility, myocarditis, chronic kidney lesions, pernicious anemia, arteriosclerosis and such complications as affect the ears, eyes, teeth, genitalia and skin require the indicated corrective measures. Coma is an emergency complication calling for expert attention. Retinitis and lipemia retinalis are relieved promptly with the control of hyperglycemia. Cataract may occur at any age if the diabetes has been relatively severe or of long standing; under insulin treatment some of the lenticular haziness occasionally improves.—I. B.

Essentials for the diagnosis of diabetes mellitus. Jonas, L., Penn. M. J. **33**: 365. 1930.

The two cardinal objective symptoms in a frank case of diabetes mellitus are glycosuria and hyperglycemia. As a rule, definite subjective symptoms with a glycosuria suggest diabetes. The diagnosis, however, should not depend solely upon glycosuria, for many subjects of glycosuria are non-diabetic. Among these are renal glycosuria and so-called alimentary glycosuria. The differential diagnosis between diabetic glycosuria and non-diabetic glycosuria is often difficult in very mild cases, but a family history of diabetes is significant, although cases of benign glycosuria have been found in families with a marked diabetic history. Generally speaking, the safest procedure when in doubt is to make periodic examination of these patients. In conclusion, Jonas states that there is no single symptom, either subjective or objective, on which the diagnosis of diabetes can be made, with the possible exception of hyperglycemia after fasting from 8 to 12 hours. The sugar tolerance test is the best readily available method for differentiating diabetes from benign glycosuria. Blood sugar within the normal fasting range two hours after taking 100 grams of glucose in untreated cases is evidence that the patient has not diabetes.—I. B.

The significance of ketogenesis. Macallum, A. B., Canad. M. A. J. **22**: 3. 1930.

Stress is laid on the relative insolubility and non-diffusibility of fatty acids until oxidised to the stage of butyric acid and its oxidation products. The cell-supply of oxygen is limited. Normally simultaneous oxidation of glucose limits the oxygen available for fat, so that so little concentration of butyric acid can occur that it and its products are almost completely oxidised. In diabetic or prolonged fasting conditions nearly all the oxygen reaching the cell is available for fat-oxidation and relatively large amounts of the two ketone-acids are produced, so that considerable quantities may pass into the blood and eventually into the urine. If butyric acid and its products were as little soluble and diffusible as caproic acid and its corresponding oxidation products, glycosuria would occur in diabetes, but no acidosis, and there would be no danger in coma.—A. T. C.

Functional dysinsulinism with epileptiform seizures. Nielsen, J. M. and E. L. Eggleston, J. A. M. A. **94**: 860. 1930.

Three cases of "epilepsy" due to dysinsulinism or hyposuprarenalism were treated, with frequent feedings or with suprarenal gland or with both, and the attacks of unconsciousness have ceased. In one case there had occurred twelve, in another more than 100, complete seizures with many petit mal attacks; yet all attacks ceased under this treatment. The period of observation in the third case is not yet long enough to justify absolute conclusions. The starvation blood sugar (taken before breakfast one morning) is not always or in all cases an index of the prevailing low point in the patient studied, especially in cases of functional dysinsulinism. In cases of functional dysinsulinism the blood sugar may rise or fall markedly without any premonitory sign that we can at present detect. The degree of increase in blood pressure under the influence of epinephrine is not necessarily any indication that the blood sugar has risen, or vice versa. Frequent feeding alone may suffice in these cases to prevent epileptiform seizures, but frequent feeding plus suprarenal gland by mouth is a surer way of maintaining sufficient blood sugar to prevent attacks. Another group of cases has thus been subtracted from the large unknown group of idiopathic epilepsy, again emphasizing that even in the most hopeless maladies we are never justified in not attempting to give relief. The treatment outlined has had no effect whatever in cases of idiopathic epilepsy.—A. M. A.

The hypoglycemia hazard in the treatment of diabetes mellitus. McCrae, T., M. Clin. N. Amer. **13**: 1013. 1930.

In certain diabetics hypoglycemia calls for real concern. Children and undernourished adults are most susceptible. On the other hand, permitting hyperglycemia and even glycosuria to continue as a prophylactic of hypoglycemia may make a severe case of diabetes out of a mild one. The level of blood sugar at which hypoglycemia develops varies. While John has found blood sugar within or above normal in 10 patients presenting symptoms of hypoglycemia, Joslin's patient with a blood sugar of .030 per cent was free from complaints. In the average patient, symptoms may be expected when the blood sugar falls below .060 per cent. The factors affecting the level of blood sugar and the insulin requirement are many, the most important being accuracy in diet and insulin administration, infection, acidosis and exercise. The incidence of hypoglycemia is reduced to a minimum and the dangers are practically nil if the simple rules for changing of dosage and distribution of insulin are observed, parallelism of the carbohydrate content of the corresponding meals maintained, and the daily exercise kept nearly uniform in time and amount.—I. B.

Effect of insulin on alimentary lipemia in normal dogs. Rony, H. R. and T. T. Ching, Proc. Soc. Exper. Biol. & Med. **27**: 533. 1930.

In dogs, both insulin subcutaneously and glucose orally prevented the alimentary lipemia ordinarily occurring after a meal of 2 cc. of olive oil per pound body weight, by stomach tube.—M. O. L.

Diabetic neuritis with paralysis. Root, H. F. and M. H. Rogers, New England J. M. **202**: 1049. 1930.

Eleven cases of diabetic "neuritis" with motor paralysis as well as sensory symptoms are reported and a classification of the common causes of pain in the legs of diabetics is given. Diabetes exerts some specific toxic effect upon the spinal cord or peripheral nerves dependent primarily upon the abnormal nutrition of inadequately controlled stages of the disease, but favored by the degenerative changes consequent upon advancing years and vascular disease. An increase in the total protein of the cerebrospinal fluid was observed in four cases. Treatment is successful and prognosis is ultimately good. Diabetes should be suspected in cases of obscure pain and paralysis of the legs just as it is in the presence of gangrene, furunculosis, or the classical symptoms of the disease.—J. C. D.

Arteriosclerosis in the young diabetic patient. Shepardson, H. C., Arch. Int. Med. **45**: 674. 1930.

A group of 50 diabetic patients who had had the disease for at least five years and who were under 40 years of age was studied to determine the incidence of arteriosclerosis as evidenced by roentgen rays. The pathogenesis of vascular disease occurring so commonly in diabetes was also investigated. The average age of the entire group was 23.4 years, and the average duration of the disease was 6.9 years. Eighteen cases, or 36 per cent, gave roentgenologic evidence of vascular sclerosis. The data obtained in this investigation are summarized in six tables. Neither the severity of the diseases nor the presence of associated pathologic changes, with the possible exception of tuberculosis, can be considered as a pathogenic factor in the development of arteriosclerosis in diabetes. The duration of the disease is important only because the causative factor must act over a reasonable period of time before its effects are manifest. The average values of blood cholesterol found in this group were markedly lower than those heretofore obtained, and, paralleling the reduction of lipemia, the incidence of arteriosclerosis was found to be greatly reduced. The definite lessening of the intensity of the damage resulting from prolonged exposure to diabetes, consequent on the addition of insulin to diabetic therapy, has resulted in a marked lowering of the average blood lipoid content. The parallel reduction in the incidence of arteriosclerosis apparently necessitates the assumption that altered fat metabolism is the morbific factor in the development of vascular disease in association with diabetes mellitus.

—Author's Summary.

The increased tolerance of pregnant rabbits for insulin. Smith, G. V. S. and G. A. Marks, Surg. Gynec. Obst. **50**: 586. 1930.

Pregnant rabbits in the latter third of their gestation period have a greater tolerance for insulin than do non-pregnant rabbits.—M. O. L.

Anatomical and functional modifications of the pancreas in different sexual states of the female (Contributo alla conoscenza delle modificazioni anatomiche e funzionali del pancreas in rapporto ad alcuni stati della vita genitale femminile). Spirito F. Arch. ostet, e ginec. **16**: 1030. 1929.

The author made both chemical and histological studies of the insular tissue of the pancreas in pregnancy and following castration. Hogs, dogs, rabbits and guinea pigs furnished the material. Evidence of hyperfunction was found in both states, being greater in the castrates.—R. G. H.

The effect of insulin on pathologic glycogen deposits in diabetes mellitus. Warren, S., Am. J. M. Sc. **179**: 482. 1930.

The tissues were stained by Best's carmine stain or Langhans iodin method. The pathologic deposits of glycogen tend to disappear in insulin-treated diabetics. The glycogenic infiltration of the liver cell nuclei, heart, pancreatic duct cells, kidneys, and granules of leukocytes was marked in diabetics. The glycogen content of the skin and voluntary muscle was decreased by diabetes.—E. L.

Cholesterol of the blood of diabetic children. White, Priscilla and Hazel Hunt, New England J. M. **202**: 607. 1930.

The study is based on 110 diabetic children. The results are summarized under twelve conclusions. Excess of cholesterol is the exception. Severe acidosis, overnutrition, extreme variations of weight, and possibly excess fat in the diet are associated with an increased cholesterol. Age is a factor. The duration of the disease, glycosuria, blood sugar and complications are not directly correlated with the blood cholesterol. In cases of decreasing severity, the cholesterol value tends to decrease.—J. C. D.

The clinical syndrome of hyperparathyroidism. Barr, D. P. and H. A. Bulger, Am. J. M. Sc. **179**: 449. 1930.

From an extensive review of the literature and a study of five cases personally the authors conclude that the symptoms of clinical hyperparathyroidism are similar to those produced by the experimental injection of excessive amounts

of parathormone. They include hypotonia and diminished electrical excitability of muscles, decalcification of bones, hypercalcemia and abnormal excretion of calcium in the urine. In some cases there is nephrolithiasis. Hypophosphatemia has been observed. Hypercalcemia is the most significant clinical sign in the diagnosis of hyperparathyroidism. Although it may be found in few other conditions, its presence usually indicates increased function of the parathyroid glands. Hyperplasia of the parathyroids and clinical evidence of hyperparathyroidism have been found in many cases of generalized bone disease, including rickets, puerperal osteomalacia, multiple myeloma and carcinomatous metastases to bones. The parathyroid changes appear to be secondary to the changes in bone. While in some cases the increased function of the parathyroids may possibly serve a useful function, in other cases it becomes actually harmful by increasing the decalcification of the bones. In generalized ostitis fibrosa cystica (von Recklinhausen's disease) the clinical picture of hyperparathyroidism is most frequently encountered. It may possibly be primary and is unquestionably harmful. In such cases removal of parathyroid tissue has accomplished clinical improvement and apparent arrest of the progress of the bone disease. Determinations of the calcium and phosphate content of the serum should be made in all cases of generalized bone disease not only as a matter of interest, but because of their therapeutic indications.—R. G. H.

Osteitis fibrosa cystica (Osteomalacia?) with evidence of hyperactivity of parathyroid bodies. Case. Bauer, W., F. Albright and J. C. Aub, J. Clin. Investigation, **8**: 229. 1930.

The authors studied calcium, phosphorus and nitrogen on the same patient. They found his negative calcium balance on a low calcium diet was markedly increased over that found in normal controls, the urinary calcium excretion high, and the fecal calcium excretion low. The data regarding the calcium metabolism, like the blood serum, are compared with similar data in a man receiving 100 units of parathyroid extract-Collip a day and are found to be almost identical. The calcium abnormalities were unaffected by the removal of two apparently normal parathyroid glands. Because the pathologic physiology in this case is similar to that in an individual receiving large doses of parathyroid extract-Collip and diametrically opposite to that in a patient with parathyriod tetany, they feel justified in concurring in the diagnosis of hyperparathyroidism. It is suggested that a high phosphorus diet might be more efficacious from a therapeutic standpoint than a high calcium diet in this case.
—R. R. Hannon.

Experimental chronic hyperparathyroidism in dogs without hypercalcemia. Bodansky, A. and H. L. Jaffe, Proc. Soc. Exper. Biol. & Med. **27**: 797. 1930.

In 11 growing dogs experimental hyperparathyroidism was produced by daily injections of parathormone. The first injection raised the serum calcium to 15 or 16 mgm. per cent, later larger doses could be given with only a temporary elevation of serum calcium. When the calcium reserves were allowed to replenish, the injection of parathormone again had the usual effect of hypercalcemia. The authors emphasize that hyperparathyroidism without hypercalcemia may exist in patients. Such a condition can be recognized by a negative calcium balance in the absence of hypercalcemia.—M. O. L.

Viosterol (irradiated ergosterol) in treatment of parathyroid tetany. Brougher, J. C., J. A. M. A. **94**: 471. 1930.

Four patients who developed a parathyroid deficiency after bilateral subtotal lobectomy were relieved of tetany by the administration of cod liver oil and subsequently viosterol. Two of these patients did not develop tetany until pregnancy. A fifth patient who developed tetany after an extensive intestinal resection was benefited by the use of viosterol.—A. M. A.

The effect of desiccated spleen and splenectomy on serum calcium in normal and parathyroidectomized dogs. Brougher, J. C., Am. J. Physiol. **92**: 648. 1930.

Splenectomy in normal and recovered thyro-parathyroidectomized dogs produced a fall in serum calcium. Desiccated spleen caused an elevation in serum calcium in splenectomized animals but not in parathyroidectomized ani-

mals. There seems to be an interrelationship between serum calcium, the spleen and the parathyroids, but it cannot be said that the spleen compensates for the loss of the parathyroids.—Author's Summary.

Concerning the functional test of the pancreatic islets in diabetics (Uber die Funktionspinfung des Inselorgans bei Diabetikem; Untersuchungen im capillaren und venösen Blut nach Zuckerbelastung und nach Insulinzufuhr). Depisch, F. and R. Hasenöhrl, Klin. Wchnschr. **8**: 1943. 1929.

In most diabetics the difference between the capillary and venous blood sugar after loading with sugar is less than in normal people. The insulin test with simultaneous determinations of the capillary and venous blood sugar is recommended for the recognition of isolated derangements of counter-regulation in the liver and in the tissues. On the basis of the insulin test there is a distinguishable difference between a hepatic and a peripheral or tissue resistance to insulin.—J. Gagnon.

Osteitis fibrosa cystica (Osteomalacia?) with evidence of hyperactivity of parathyroid bodies. Case. Hannon, R. R., E. Shorr, W. S. McClellan and E. F. DuBois, J. Clin. Investigation, **8**: 215. 1930.

The report of a case which, from clinical and roentgenological studies, appears to be due to osteitis fibrosa cystica. There is a long clinical history of progressive skeletal deformities with frequent fractures which healed slowly, general rarefaction of the bones with no proliferation and some cyst formation. There had been no improvement from dietary, vitamin D, and ultraviolet therapy. Parathyroid extract seemed to aggravate the condition. Blood calcium was elevated, ranging from 13.4 to 16.5 mgm. per 100 cc. blood The blood phosphorus was low between 1.1 to 3.3 mgm. per cent and mostly below 2.5 mgm. Calcium required daily to maintain him in calcium equilibrium was 0.7 mgm., whereas 0.4 gm. is usually sufficient for a normal individual. Seventy to 90 per cent of the calcium was lost in the urine, which is the reverse of normal, and showed good absorption but poor retention of the calcium. The electrical reactions revealed a marked reduction in excitability of muscle and nerve. The conclusion was that the underlying basis for the osteitis fibrosa cystica in this subject was a hyperactivity of the parathyroid bodies.—R. R. Hannon.

Osteitis fibrosa cystica (Osteomalacia?) with evidence of hyperactivity of parathyriod bodies. Case. McClellan, W. S. and R. R. Hannon, J. Clin. Investigation, **8**: 249. 1930.

Calcium and phosphorus balances are presented by McClellan and Hannon for the previously reported case, which was observed continuously for 154 days. Distinct improvement in the patient's physical condition occurred during his stay in the hospital. An intake of 1 gm. of calcium was found necessary to keep him in positive calcium balance. The positive balance was increased by increasing the intake. No definite benefit could be ascribed to cod liver oil or quartz lamp therapy. Thyroid and pituitary extracts diminished the amount of calcium retained. The excretion of calcium in the urine was not affected by increased intake of calcium, but was increased as a result of giving thyroid extract. The excretion of calcium in the feces was elevated by increasing the intake, and there is suggestive evidence that it was slightly increased by giving pituitary extracts. The excretion of phosphorus in the urine was not significantly affected by either the intake or glandular therapy. The phosphorus in the feces varied with the intake. A positive phosphorus balance was maintained throughout the entire period of observation even in those periods in which there was definite loss of calcium from the body. The removal of two parathyroid glands caused only slight changes in the levels of serum calcium and phosphorus and no change in the basal metabolic rate.—R. R. Hannon.

Glycogen content in the liver of animals injected with Collip's parathyroid extract (Sur la teneur du foie en glycogène chez les animaux recevant en injection de l'extrait parathyroïdien de Collip). Parhon, C. I. and M. Cahane, Compt. rend. Soc. de biol. **101**: 1179. 1929.

In guinea pigs there is a slight but not constant increase of glycogen in the injected animals.—J. C. D.

The effect of parathyroid extracts upon the blood picture (Uber die Wirkung des Parathyreoideaextraktes auf das Blutbild). Pellathy, S. v. and J. v. Fernbach, Endokrinologie, **3**: 406. 1929.

Parathyroid extracts administered subcutaneously increased the number of myeloid cells. The effects seem to be through the nervous system rather than due to blood calcium. The effect is sympathotonic. It should be useful in vagotonic dieases, such as asthma.—B. C.

Tetany associated with arrested growth and striation of bones. Stannus, H. S., Proc. Roy. Soc. Med. **23**: 69. 1930. (Clin. Sect.)

The patient was a boy 15½ years old who, in January, 1930, after some "upset," began to cry. This was immediately followed by respiratory spasm with contraction of the muscles of the chest and neck. Four days later a second such attack occurred in which the hands were also affected. Since then the spasms have occurred 2 to 3 times each evening. A diagnosis of tetany was made and a spasm was easily induced at will by causing the boy to breathe forcibly for 2 or 3 minutes and could be cut short by an injection of a few drops of a 5 per cent solution of calcium chloride into a vein. Skiographic examination showed some transverse striation at the lower end of the shaft of the tibia. The author remarks that in this case there has been a deficiency of vitamin D in the diet.—I. B.

Morphological contributions to the question of the endocrine function of the epiphysis (Morphologische Beitrage zur Frage der endokrinen Funktion der Epiphyse). Brandenburg, E. v., Endokrinologie, **4**: 81. 1929.

On a basis of 157 human and 82 pig pineals studied, the writer concludes that the work of Aschner is erroneous and that there is no relationship of pineal shape to sex; no relationship of shape to pregnancy; and that there is no relation between the calcium content of the gland and pregnancy—or even sex. —B. C.

The geographic distribution of goiter in Russia (Uber die geographische Verbreitung des Kropfes in Russland). Arndt, H. S., Endokrinologie, **4**: 176. 1929.

Goiter distribution in Russia shows that it is not racial, and further studies indicate there is no "racial disposition"; in other words, the causal factor is external to the individual, possibly in the food or water supply which may be short in iodine content. Geological formations are discussed in this relation but conclusive evidence seems absent.—B. C.

Sympathetic activity after prolonged administration of thyroxin. Blau, N. F. and Helen McNamara, Proc. Soc. Exper. Biol. & Med. **27**: 997. 1930.

Large cats were made hyperthyroid by treatment with thyroxin for 35 to 57 days. In these and in normal cats under paraldehyde anesthesia, blood pressure tracings were made before and after the intravenous injection of .003 mgm. per kilo of adrenaline chloride. The rise in blood pressure averaged 106 per cent higher in the hyperthyroid cats than in the normal ones.—M. O. L.

Carcinoma of thyroid with metastases. Buxton, J. D., Proc. Roy. Soc. Med. **23**: 58. 1930. (Sect. Surg.)

This specimen was removed at autopsy from a woman aged 53, who came to the hospital because she had broken her arm. She had a thyroid tumor, which she said had been present for 2 years, and there was a large swelling on the skull which had been there for a year. At the autopsy there were found the large tumor of the skull and two secondary deposits in the jaw; the right humerus was infiltrated with growth, and two pathological fractures were present. There was a secondary deposit in the lower end of one femur. The thyroid was carcinomatous and the involved bones showed carcinoma but no colloid.—I. B.

Some notes of our present knowledge and ignorance of thyroid function. Cameron, A. T., Canad. M. A. J. **22**: 240. 1930.

A review dealing with the chemistry of the thyroid, the general distribution of iodine, the prophylactic use of iodine, and the pre-operative treatment of thyroid cases with Lugol's solution.—Author's Abst.

Blood volume in hyperthyroidism. Chang, H. S., Proc. Soc. Exper. Biol. & Med. **27**: 881. 1930.

In 17 cases of exophthalmic goiter and one of toxic adenoma the total blood volume, measured by the CO method, was somewhat increased over the normal. In 14 patients after subtotal thyroidectomies the total blood volume decreased from 7 to 28 per cent. Treatment with Lugol's solution diminished the blood volume along with the drop in basal metabolism.—M. O. L.

The treatment of toxic thyroid with rays of short wave length. Clement, G., Radiol. Rev. & Chicago M. Rec. **52**: 65. 1930. Abst., Arch. Physical Therapy, **11**: 142.

Before 1903 the treatment of the toxic thyroid was almost entirely medical. Since 1903 it has been largely surgical. From about 1910 to the present time, radiation, either by x-ray or radium, has been advocated and is slowly but surely gaining ground. Statistics show that about the same number of patients are benefited by radiation as by surgery. Two types of radiation are presented. One case is reported showing what may be accomplished by radiation. The author feels that the patient with toxic thyroid should be given the advantage of radiation therapy, since the treatment causes no pain, no scar, little or no loss of time from hospitalization, no operative mortality, and because the results are as good as by any other method of treatment.

Hyperthyroidism and pregnancy. Clute, H. M. and D. H. Daniels, Am. J. M. Sc. **179**: 477. 1930.

In the Lahey Clinic, Boston, the incidence of pregnancy in 3,678 cases of hyperthyroidism was 0.41 per cent. From a study of this material it is concluded that special care is needed that the normal elevation of metabolism in late pregnancy is not interpreted as evidence of thyroid disease. Hyperthyroidism does not cause an unnatural termination of the pregnancy in the majority of cases when it is properly treated. It is believed that pregnancy does not increase the toxicity of primary hyperthyroidism except as the increased proplasmic mass of pregnancy brings some increase in metabolism. Pregnancy is, however, distinctly an added burden in hyperthyroidism which should be avoided if possible. Babies born of thyrotoxic mothers are not abnormal. Pregnancy does not appear to be a cause of primary hyperthyroidism. Pregnancy after thyroidectomy for primary hyperthyroidism does not cause recurrence of thyroid toxicity. Babies born of mothers who have had thyroidectomy for hyperthyroidism are normal. Thyroidectomy for primary hyperthyroidism can be undertaken during pregnancy with safety to both mother and child.—R. G. H.

Resistance to thyroxin (Uber Thyroxinresistenz). Falta, W., Endokrinologie, **5**: 62. 1929.

The author calls attention to the occasional occurrence of very high resistance to thyroxin in human subjects. Two personal cases are cited. The condition is probably to be ascribed to abnormality of the central nervous system.
—R. G. H.

Angina pectoris associated with exophthalmic goiter and hyperfunctioning adenomatous goiter. Haines, S. F. and E. J. Kepler, M. Clin. N. Amer. **13**: 1317. 1930.

This is an interesting discourse on an important clinical combination with 3 illustrated case histories. Cases of angina pectoris complicated by exophthalmic goiter or hyperfunctioning adenomatous goiter show in many instances definite improvement in the angina after thyroidectomy. The prognosis is poor unless the hyperthyroidism is controlled.—I. B.

Auricular fibrillation in patients with goitre. I. Value of quinidin based on the study of 114 cases. Hurxthal, L. M., Am. J. M. Sc. **179**: 507. 1930.

This report deals with 55 cases of auricular fibrillation which were treated at the Lahey clinic. Previously, the paroxysmal auricular fibrillation was treated with digitalis in 12-18 grain doses. This method of treatment will slow the pulse but will not exert a favorable action on stopping the paroxysms. Quinidin sulphate, three grains after breakfast is given and then six grains every two hours until the pulse is regular or unpleasant symptoms arise. No more than a total of 39 grains should be given. In the selected cases, the quinidin therapy was successful in 88 per cent. When the hyperthyroidism was uncomplicated with cardiovascular disease, this method of treatment was successful in nearly all cases.—E. L.

Changes in the adrenals after thyroidectomy (Nebennierenveränderunger bei Thyreoidektomia). Kedrowsky, W. J. and M. L. Birjukoff, Endokrinologie, **5**: 116. 1929.

Working with the sheep as experimental animal, the authors noted that thyroidectomy resulted in 70.5 per cent of the cases in extensive morphological changes in the adrenals. These were generally of a degenerative character. They seemed to occur at random in either the cortex or the medulla. No relationship could be determined between time elapsed after operation and severity of adrenal involvment.—R. G. H.

Hyperthyroidism associated with cardiac disorders. Lahey, F. H., Surg. Gynec. Obstet. **50**: 139. 1930.

Thyroidism in itself does not by its direct action on the heart produce destructive changes in the heart. That frequently associated with cardiac decompensation is atypical and of the apathetic type; this is less striking and more dangerous than thyroidism of the activating type. The possibility of restoration of cardiac capacity after removal of the associated thyroidism is extraordinary. Toxic adenomata are no more apt to cause cardiac failure than is primary hyperthyroidism or exophthalmic goiter.—A. T. C.

The affinity of haemoglobin for oxygen, expressed by the constant of dissociation k, in certain cases of hyperthyroidism (Sur l'affinité de l'hémoglobine pour l'oxygène experimée par la constante de dissociation k dans quelques cas d'hyperthyroïdies).

Note on basal metabolism and total oxygen capacity of the blood in normal cases, anemics, and those with hyperthyroidism (Du rapport du métabolisme basal et de la capacité totale en oxygène du sang chez lest sujects normaux, les anémiques et les hyperthyroïdiens). Litarczek, G., H. Aubert and I. Cosmuesco, Compt. rend. Soc. de biol. **102**: 157, 159. 1929.

Studies are reported on the relations between the oxygen demands of the tissues and the supply carried in the blood. In anaemias the blood is oxygen poor, while in hyperthyroidism there is increased demand by the tissues, so that in both diseases there is an upset of the oxygen balance of the same kind. Tables and formulae of these relations are given.—J. C. D.

Effects of thyroidectomy and thyroxinization on the protein balance of the serum (L'influence de la thyroïdectomie et de la thyroxinisation sur l'équilibre portéique du sérum). Loeper, M., A. LeMaire, A. Lesure and J. Tonnet, Compt. rend. Soc. de biol. **101**: 856. 1929.

Thyroidectomy in dogs reduces and thyroxinization increases the amount of serine in the blood of dogs. This is further evidence of a protein controlling action of the thyroid.—J. C. D.

The use of the planimeter for measuring the degree of evolution and functional condition of the thyroid (Emploi du planimètre pour apprécier l'évolution de la thyroïde et sa valeur fonctionnelle). Marza, E. and V. Marza, Compt. rend. Soc. de biol. **101:** 1190. 1929.

By obtaining an actual measure of the area of the follicles and the height of the epithelium, the condition of the thyroid can be accurately recorded.
—J. C. D.

Thyroid extract in treatment of nephrosis. McClendon, S. J., J. A. M. A. **94:** 1202. 1930. Abst. A. M. A.

The three cases of nephrosis reported by McClendon demonstrate the effect of thyroid therapy in the management of the disease. These cases would seem to show that: 1. Dietetic therapy and the treatment of the existing sinus conditions, or other upper respiratory infection, while important and necessary adjuncts in the treatment of nephrosis, are not sufficient in themselves to control the edema and albuminuria. 2. Thyroid extract, in adequate dosage, is an effective therapeutic agent in the management of the true nephrosis.

The sedimentation velocity of erythrocytes in thyrotoxicosis. Mora, J. M. and J. T. Gault, J. Lab. & Clin. Med. **23:** 586. 1930.

The sedimentation speed of erythrocytes was studied in 30 cases of thyrotoxicosis, by the Merrzenmeier method, before and after thyroidectomy. The rate was increased in all cases before operation. The administration of iodine decreased the speed of sedimentation in 6 out of 11 cases, and increased it in 5 cases. Thyroidectomy was followed by no increased rate in 13 cases, and by a decreased speed in 14 cases. There seemed to be little parallelism between the sedimentation velocity, the basal metabolic rate, and the clinical picture.
—I. B.

The significance of abnormal metabolic features in the management of thyrotoxicosis. Palmer, W. B., Ann. Int. Med. **3:** 651. 1930.

This report is from the Presbyterian Hospital (N. Y.), where the combined medical and surgical staff decide as to whether the patient shall receive medical or surgical treatment. Basal metabolism determinations are an index of the severity of the thyrotoxicosis, but clinical judgment must also be considered because of discrepancies between the clinical condition and the metabolic rate. Nitrogen equilibrium should be established. This may require 75-100 per cent above the caloric intake as determined by the basal metabolism tests. Every effort should be made to give sufficient food to produce a gain in weight. The laboratory studies (B. M. R., mineral balance, etc.) are of aid but should be interpreted in the light of clinical judgment.—E. L.

Recurring exophthalmic goiter. Pemberton, J. D., J. A. M. A. **94:** 1483. 1930. Abst., A. M. A.

Of the 878 patients with exophthalmic goiter operated on in the Mayo Clinic during the first 11 months of 1929, the author says five died, a mortality of 0.56 per cent. Of the 1,683 patients with exophthalmic goiter operated on in the Mayo Clinic in 1920, 1921 and 1922, 50 (2.9 per cent) had returned up to September 1, 1929, on account of the development of recurrent symptoms that warranted further surgical treatment. On account of this tendency to recurrence in a small percentage of patients with exophthalmic goiter many surgeons, in order to avoid recurrence of hyperthyroidism, have advocated an extremely radical operation, but Pemberton says he has never seen any convincing data submitted to demonstrate that the results of the radical operation are better than those of the conservative resection. A study of the records of 100 consecutive operations on patients with recurrent hyperthyroidism in exophthalmic goiter in whom previous operation on the thyroid gland had been done in the Mayo Clinic revealed that the average interval of time between the primary operation and the onset of recurring symptoms was 5.4 years, and the longest interval 21 years. The average interval between the first and second operation was 6.66 years. Of the 26 patients who had a recurrence within 12 months, in 9 the interval of time was so brief and the onset so indefinite that it was at least suggestive that the patient never had been entirely free from the disease.

Although there was growth of the remnant of tissue preserved at operation, Pemberton avers that the contention that recurrence of the hyperthyroidism of exophthalmic goiter is wholly attributable to inadequate resection of the gland and that its prevention can be accomplished by more radical resection, even to the point of the production of hypothyroidism, cannot be substantiated by the facts. He believes that the removal of from 65 to 85 per cent of the gland is adequate in a large percentage of cases and that the preservation of a posteromesial portion on each side of the trachea equivalent to from one-sixth to two-thirds of a normal lobe will afford ample protection against injury to the nerves and parathyroid bodies.

Myxedema during the administration of iodin in exophthalmic goiter. Thompson, W. O., Phebe K. Thompson, A. G. Brailey and A. C. Cohen, Am. J. M. Sc. **179**: 733. 1930.

Myxedema was produced in four patients by the administration of iodin after a subtotal thyroidectomy for exophthalmic goiter. The myxedema could be made to disappear by omitting the iodin or by giving thyroid in addition to the iodin.—E. L.

The range of effective iodine dosage in exophthalmic goiter. III. The effect on basal metabolism of the daily administration of one-quarter drop of compound solution of iodine and of slightly smaller doses, with a summary of results to date. Thompson, W. O., A. C. Cohen, Phebe K. Thompson, E. G. Thorp and A. G. Brailey, Arch. Int. Med. **45**: 430. 1930.

During the daily administration of one-fourth drop of compound solution of iodine to 14 unselected hospital patients with exophthalmic goiter, 7 showed a reduction in basal metabolism of from 10 to 26 points, 6 showed no significant change and one showed an increase. During the administration of one-fifth drop daily to 2 hospital patients with the disease, one showed a reduction of 14 points and the other showed no change. In the one-fourth drop series, the basal metabolism was only slightly lower, and in the 2 hospital patients who received 1.5 drop, no lower during the subsequent administration of 30 drops a day, than during the administration of the small doses. Whereas only 50 per cent of the patients showed a reduction in basal metabolism of 10 points or more during the daily administration of one-fourth drop, 65 per cent showed a reduction during the daily administration of one-half drop, and 88 per cent during the daily administration of 1 drop. The administration of one-fourth drop a day caused an average reduction in basal metabolism of only 9 points (from plus 43 to plus 34 per cent) as compared with 14 points (from plus 40 to plus 26 per cent) for one-half drop and 27 points (from plus 36 to plus 19 per cent) for 1 drop. In the 7 patients who responded to one-fourth drop, the maximum reduction in basal metabolism occurred on the average in 5 days. In 1 patient it had started within 24 hours.

In three of the cases observed, the reaction to iodine appeared to be reversible, the administration of one-fourth to one-half a drop of compound solution daily being associated with an increase in the basal metabolism and in the severity of the disease, and the immediate subsequent administration of large doses being associated with a decrease in both factors. Doses as small as one-fourth and one-half drop of compound solution of iodine a day, even when they are too small to cause a reduction in basal metabolism, may sometimes interfere with the effect of much larger doses given immediately afterward. In mild cases of the disease, this phenomenon does not seem to occur. A comparison of the effects of various doses of iodine, therefore, can be made only by giving each dose to untreated patients with the disease. It is also essential to secure a resting level of basal metabolism before iodine is started. In the routine pre-operative treatment of exophthalmic goiter it is desirable to give suddenly an adequate excess of iodine and not to precede this with small doses.

—Authors' Summary.

Increased metabolism only one factor in the production and maintenance of the hyperglycemia and glycosuria in experimental hyperthyroidism. Shpiner, L. B., Am. J. Physiol. **92**: 672. 1930.

Large doses of thyroid extract do not produce a hyperglycemia and glycosuria in normal dogs. However, in a series of six dogs which had the major

portion of their pancreas removed with the factor of safety reduced to a minimum, it was effective in the production of a permanent hyperglycemia and glycosuria (diabetes). The greater hyperpyrexia which accompanies the subcutaneous injection of sodium nucleinate produces a mild hyperglycemia and glycosuria in normal dogs. In a series of four partially pancreatectomized dogs sodium nucleinate did not cause as marked and persistent a hyperglycemia and glycosuria as did thyroid feeding. The results seem to show that the influence of the thyroid is not solely through its effect on basal metabolism, but possibly through some toxic effect of thyroxin exerted on the islet tissue of the pancreas. In this sense (toxic action of the thyroid hormone), one might speak of an antagonism between the pancreas and the thyroid.—Author's Summary.

A histological and biochemical study of pathological thyroid material, with special reference to the effect of Lugol's solution. Wheeler, D., Canad. M. A. J. **22:** 157. 1930.

The paper gives the results in a series of 126 cases, some two-thirds of which had received treatment with Lugol's solution prior to thyroidectomy. The thyroids were examined immediately. Parts of each gland were examined histologically, and the remainder analyzed for water, fat, nitrogen, and iodine content. The results were critically analyzed both from the viewpoint of clinical diagnosis and from the actual histological appearance. Wheeler finds that the thyroid gland, whatever its type, shows an increased iodine content after the patient has received a course of Lugol's solution. Those which after treatment present a colloid appearance have a high iodine content, and in such colloid glands there seems to be some relation between this iodine content and the amount of iodine administered to the patient. Such relationship does not exist for non-colloid glands. Nor does the same dosage of iodine (as Lugol's solution) appear to have the same effect on the histology of different glands. Glands in cases of toxic adenoma or Graves' disease that have not received the iodine treatment show a relatively low iodine-content, while those of the same group which after treatment retain histologically toxic characteristics show an intermediate value. The iodine content of a toxic gland increases proportionately as the gland approximates to the colloid picture.—A. T. C.

The effect of the daily administration of iodine on the calorigenic action of single intravenous injections of thyroxine. Wilhelmj, C. M. and W. M. Boothby, Am. J. Physiol. **92:** 568. 1930.

The daily oral administration of iodine for 17 and 22 days before and for 8 days after a single intravenous injection of 10 mgm. of thyroxine (in a dog) did not influence the calorigenic action of thyroxine. Following the injection of thyroxine the basal heat production rose rapidly and reached its maximal height in from 22 to 70 hours; following this there was a progressive decrease in heat production which reached the original basal level in about 190 hours (8 days). In three control experiments in which iodine was not given the extra heat production averaged 300 calories, and in two experiments in which iodine was given the average was 311 calories. The response of the same animal to repeated single injections of 10 mgm. of thyroxine was constant; the average extra heat production in five experiments amounted to 304 calories, and the maximal and minimal values obtained were within ± 8 per cent of this average. The daily oral administration of iodine (2 cc. of the compound solution of iodine) was without appreciable influence on the basal level of heat production.—Authors' Summary.

Mild mania on recovering from myxedema. Ziegler, L. H., M. Clin. N. Amer. **13:** 1368. 1930.

The patient was a woman of 58 whose complaints were loss of strength, especially in the legs; nervousness of more than 1 year's duration; loss of 30 pounds in weight, intolerance to heat, and excessive perspiration. The basal metabolism rate was moderately elevated. A diagnosis of exophthalmic goiter was followed by subtotal thyroidectomy, with a report of "hypertrophic parenchymatous thyroid gland." The patient gained weight up to 40 pounds above normal, felt sluggish and unusually sleepy. The basal metabolism rate was —29. Desiccated thyroid was administered. With rising metabolism rate, the patient became very restless, talkative, distractible, rambling in conversation,

and showed flight of ideas. There was no depression. The threshold of excitability was lowered. As the basal metabolism rate approached normal, her normal personality returned. She lost her excess fat and was not depressed except at short intervals just before she became normal when she wept at times and complained of loneliness. The author concludes that in this case, with the patient always talkative and energetic, myxedema served to depress natural tendencies to expression. On releasing her from this depressing influence by elevating the basal metabolism rate, her natural tendencies to activity and talk became exaggerated, and assumed the clinical proportions of mild mania.—I. B.